TO STUDY DIFFERENT CLINICAL PHENOTYPES AND SHORT TERM FOLLOW UP IN PATIENTS PRESENTING WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION

A THESIS SUBMITTED TO

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT (PUNJAB)

IN THE PARTIAL FULFILLMENT

FOR THE AWARD OF DEGREE OF

DM

IN

CARDIOLOGY

2024

Submitted By

DR BHOJ RAJ SHARMA

DEPARTMENT OF CARDIOLOGY
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA,PUNJAB

DECLARATION BY THE CANDIDATE

I hereby declare that the thesis entitled "**TO STUDY DIFFERENT CLINICAL PHENOTYPES AND SHORT TERM FOLLOW UP IN PATIENTS PRESENTING WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION**" submitted towards partial fulfillment of the requirements for the award of **DM in Cardiology** degree to BFUHS is a compilation of original work carried out by me under the supervision of **Dr. Gurpreet S Wander**, Principal & Professor, Department of Cardiology and **Dr. Gautam Singal**, Associate Professor, Department of Cardiology. No part of this thesis has formed the basis for the award of any degree previously.

_____

Dr. Bhoj Raj Sharma
Department of Cardiology
Dayanand Medical College & Hospital,
Ludhiana, Punjab

Date:

Place:

CERTIFICATE OF SUPERVISORS

This is to certify that the work incorporated in this thesis entitled "**TO STUDY DIFFERENT CLINICAL PHENOTYPES AND SHORT TERM FOLLOW UP IN PATIENTS PRESENTING WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION"** has been carried out by **Dr. Bhoj Raj Sharma** under our direct supervision. The data incorporated in this thesis is original and genuine and has been carried out by the candidate himself.

Signature of Supervisor

Dr. Gurpreet S Wander
Principal & Professor
Department of Cardiology
DMC&H, Ludhiana

Signature of Co-Supervisor

Dr. Gautam Singal
Associate Professor
Department of Cardiology
DMC&H, Ludhiana

Date:

ENDORSEMENT BY THE HEAD OF THE INSTITUTE

This is to certify that the thesis entitled "**TO STUDY DIFFERENT CLINICAL PHENOTYPES AND SHORT TERM FOLLOW UP IN PATIENTS PRESENTING WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION"** is a bonafide research work done by **Dr. Bhoj Raj Sharma** under the supervision of **Dr. Gurpreet S Wander**, Principal & Professor, Department of Cardiology and **Dr. Gautam Singal**, Associate Professor, Department of Cardiology in this institution.

Principal

Dr. G S Wander
Principal
DMC&H, Ludhiana

Date:

COPYRIGHT

Declaration by the Candidate

I hereby declare that the Baba Farid University of Heath Sciences, Faridkot, shall have the rights to preserve & use this thesis in print or electronic format for academic/study purpose by the research scholar/students.

Signature

Dr. Bhoj Raj Sharma
Department of Cardiology
Dayanand Medical College & Hospital,
Ludhiana, Punjab - 141001

Date:

© Baba Farid University of Health Sciences, Faridkot

Dedicated

To

My Teachers

&

Parents

ACKNOWLEDGEMENT

I am deeply humbled to have completed this significant milestone in my academic journey, and I am compelled to express my heartfelt gratitude to the individuals who have supported me throughout this endeavor.

I praise God the Almighty, merciful and passionate for his showers of blessings, unparalleled grace and granting me the capability to proceed successfully and in good health. I express my sincere gratitude and sense of indebtedness to my teacher and supervisor, ***Dr. Gurpreet Singh Wander****, Professor, Department of Cardiology, Dayanand Medical College and Hospital, Ludhiana, whose extraordinary wisdom, expertise, and mentorship have been the guiding light of my research journey.* ***Dr. Wander's*** *exceptional leadership and mentorship have not only shaped the direction of this work but have also inspired me to strive for excellence in my academic pursuits. His guidance has been instrumental in helping me navigate the complexities of research, and his insightful feedback has been invaluable in shaping the direction of this work. I am honored to have had the privilege of working with him and I aspire to emulate his qualities of wisdom, humility, and dedication to the pursuit of knowledge.*

Words cannot express my deepest gratitude to my distinguished mentor and co-supervisor ***Dr. Gautam Singal,*** *Associate Professor, Department of cardiology,*

Dayanand Medical College and Hospital, Ludhiana, whose limitless efforts and keen interest helped me throughout this study. I thank him for his patience and timely advice, without which I would have floundered in this study. It is indeed my extraordinary privilege to be able to work under his expert guidance. His boundless expression of knowledge, guidance and constant supervision has gone a long way in ensuring the completion of this study.

It gives me immense pleasure to express my heartiest thanks to ***Dr. Bishav Mohan****, Professor and Head, Department of Cardiology, Dayanand medical college and hospital, Ludhiana for his teaching, constant motivation and guidance in the conduct of this study. He provided the best encouragement, facilities and affection that helped me to overcome whatever obstacles came during my study.*

I would like to express my gratitude to ***Dr. Naved Aslam, Dr. Shibba Takkar Chhabra*** *and* ***Dr.Abhishek Goyal*** *, Professors, Department of Cardiology,* ***Dr. Akash Batta*** *and* ***Dr. Anshuman Gupta****, Assistant Professors Department of Cardiology. Their invaluable assistance and encouragement have been significant source of motivation through phases of research.*

I would also like to thank my parents ***Sh. Ami Lal Sharma*** *and* ***Mrs. Daya Sharma*** *whose unwavering love and belief in me have been the foundation upon which I*

have built my academic and personal life. Their countless sacrifices, patience and encouragement have always pushed me to strive for excellence. You have been my pillars of strength, and I owe so much of who I am today to the values you instilled in me. From the very first day of my education you have been my greatest supporters, and I am forever indebted to you for all that you have done.

To my beloved wife ***Dr. Neetu Verma****, I cannot express enough gratitude for your unrelenting support, understanding, and encouragement throughout this process. Your love, patience, and sacrifices have been my refuge during the many long nights and challenging days. You have stood by me through every step, offering not only emotional support but also practical help when needed. Thank you for always believing in me, even when I found it hard to believe in myself. Your presence in my life has been a constant source of motivation and joy, and I share this achievement with you as much as it is my own.*

I express my deep sense of gratitude to my brothers ***Rama Kant Sharma*** *and* ***Dr. Shashi Kant Sharma****. Your support, encouragement, and constant check-ins made this journey less daunting and more manageable. Whether it was a word of advice, a shared moment of joy, or simply knowing that you believed in me, each of*

you has contributed to this accomplishment in your own way.

I take this opportunity to thank my seniors ***Dr. Sushil Saini, Dr. Amit Gupta, Dr. Bhavuk Jaiswal,*** *my colleagues* ***Dr. Keshav Sachdeva, Dr. Sahil Bansal*** *and my juniors* ***Dr. Abhishek Garg, Dr. Tasleem Arif, Dr. Ankit Gulia , Dr. Sahil Sheokand, Dr. Anil Yadav, Dr. Himanshu Garg, Dr. Shubham Garg, Dr. Rishav Tohani, Dr. Avneesh Garg, Dr Bharat Bhushan, Dr. Raagini Gupta, Dr. Jasneet Kaur, Dr. Nikita Sharma*** *for their constant help and encouragement throughout this journey. My gracious thanks Research Department DMC&H for helping me with patient counselling and enrolment and helping me during difficult times.*

I acknowledge the help of all those invisible hands who are responsible for the successful outcome of this dissertation. My heartiest thanks to the nursing staff of the Department of cardilogy for their sincere cooperation. Last but not the least, I would like to thank all the patients who participated in this study.

With utmost sincerity, I acknowledge all patients who participated in the study, without which the completion of this dissertation would not have been possible.

Dr. Bhoj Raj Sharma

LIST OF ABBREVIATIONS

ADHF	Acute decompensated heart failure
AF	Atrial Fibrillation
ALP	Alkaline Phophatase
ALT	Alanine Transaminase
ARNI	Angiotensin receptor-neprilysin inhibitor
AST	Aspartate Tranaminase
BMI	Body Mass Index
CAD	Coronary Artery Disease
CKD	Chronic Kidney Disease
COPD	Chronic Obstructive Pulmonary Disease
CVA	Cerebrovascular accident
DM	Diabetes mellitus
EDV	End-diastolic volume
eNOS	endothelial nitric oxide synthase
ESC	European Society of Cardiology
HF	Heart Failure
HFpEF	Heart Failure with preserved ejection fraction
HFrEF	Heart Failure with reduced ejection fraction
HTN	Hypertension
IQR	Inter Quartile Range
IASD	Interatrial shunt device
IVDU	Intravenous Drug Use

IVRT	Isovolumic relaxation time
LLTS	Low-level transcutaneous vagal stimulation
LV	Left Ventricle
NO	Nitric Oxide
NP	Natriuretic Peptides
OSA	Obstructive Sleep Apnea
P- VALUE	Probability value
PA	Pulmonary artery
PAD	Peripheral arterial disease
PCV	Packed Cell Volume
PRKG1	Protein kinase CGMP-dependent 1
SD	Standard Deviation
SGLT2i	Sodium-glucose co-transporter 2 inhibitors
TGF-beta	Transforming growth factor-beta 1
TLC	Total Leucocyte Count
TNF-alpha	Tumor necrosis factor-alpha
TR	Tricuspid Regurgitation
VHD	Valvular heart disease

ABSTRACT

Background: Heart failure with preserved ejection fraction (HFpEF) is a rising health problem. The Diagnosis of HFpEF is challenging due to gaps in our understanding of the disease's pathophysiology, lack of universal diagnostic criteria, heterogeneity of HFpEF populations, presence of multiple noncardiac comorbidities, and the lack of evidence-based treatments remain significant challenges in its management.

AIM: To study different clinical phenotypes and short-term follow-up in patients presenting with presenting with preserved ejection fraction

Methods: We conducted a single-center, prospective observational study in a tertiary care center on 175 patients diagnosed with HFpEF from January 2023 to June 2024. Three phenotypes were identified, including the lean/ elderly/multimorbid; metabolic; and young CAD.

Results: The mean age was 63.45, and 65.7% were female. COMMON COMORBIDITIES AT PRESENTATION WERE (N,%) HTN (146, 83.4%), CAD (111, 63.4%), DM (67, 38.3%), AF (50, 28.6%), Hypothyroidism (12, 6.9%). The prescription rate for ACEi, ARB, ARNI, SGLT2i, diuretics, and mineralocorticoid antagonists was (50,28.6%), (84,48.0%), (16,9.1%), (47, 26.9%), (105,60%), (62,35.4%) respectively. The "lean/elderly/multimorbid" phenotype had a more severe grading of diastolic dysfunction (grade 2 and grade 3 DD =53.8% and 38.5% patients; p-value=0.047)and the worst performance of 6MWT. (mean + SD= 264m + 100.57). The "lean / elderly / multimorbid" phenotype demonstrated the highest symptom severity and hospitalization rates. (43.6% p-value =0.046)

Conclusion: Our research highlights lean/elderly/multimorbid patient population had a high disease burden. we identified three phenotypes that provided contemporary and pragmatic insights into a phenotype-guided approach,

Keywords: HFpEF, phenotypes, diastolic dysfunction, hospitalization rates, mortality

TABLE OF CONTENTS

S. NO.	TOPIC	PAGES
I	INTRODUCTION	1-11
II	AIMS AND OBJECTIVES	12
III	REVIEW OF LITERATURE	13-23
IV	MATERIALS AND METHODS	24-27
V	OBSERVATIONS AND RESULTS	28-62
VI	DISCUSSION	63-69
VII	SUMMARY AND CONCLUSION	70-73
VIII	BIBLIOGRAPHY	74-81

APPENDICES – I

- PROFORMA
- MASTER CHART

APPENDICES – II

- APPROVAL LETTER OF THESIS PLAN
- THESIS PLAN

LIST OF TABLES

Table No.	Title	Page No.
1.	NT PRO BNP Cut off	24
2.	H2FPEF Score	25
3.	HFA-PEFF Score	26
4.	Age distribution of the patients	29
5.	Gender distribution of the patients	30
6.	BMI of patients enrolled	31
7.	Distribution of Cases by Risk Factors	32
8.	Distribution of cases by comorbidities	33
9.	Distribution of Cases by Medication Class	34
10.	Distribution of Cases by NYHA Classification	35
11.	Hospitalizations Due to Heart Failure During Follow-Up	36
12.	Mortality Rates among Study Participants	37
13.	Distribution of cases according to the New York Heart Association (NYHA) functional classification at the last follow-up	38
14.	Distribution of age across phenotypes	39
15.	Distribution of sex across phenotypes	41
16.	Distribution of BMI across phenotypes	43
17.	Distribution of Alcohol and smoking across phenotypes	45
18.	Distribution of comorbidities across phenotypes	47
19.	Distribution of Cardiovascular Medications across Phenotypes: Analysis of ACEI, ARB, ARNI, SGLT2 Inhibitors, Diuretics, and MRA Usage across phenotypes	49-50
20.	Distribution of hospitalization due to heart failure during follow up across phenotypes	52
21.	Distribution of mortality across phenotypes	54

22.	Distribution of NYHA CLASS across phenotypes	56
23.	NYHA class of patients across different phenotypes (A,B and C) during last follow up visit	58
24.	Comparison of clinical, laboratory, and functional parameters across three phenotypes (A, B, and C)	60-61
25.	Comparison of diastolic dysfunction across various phenotypes (A, B and C) during start of enrolment	62

LIST OF FIGURES

Fig. No.	Title	Page No.
1.	Age distribution of the patients	29
2.	Gender distribution of the patients	30
3.	BMI of patients enrolled	31
4.	Distribution of Cases by Risk Factors	32
5.	Distribution of cases by comorbidities	33
6.	Distribution of Cases by Medication Class	34
7.	Distribution of Cases by NYHA Classification	35
8.	Hospitalizations Due to Heart Failure during Follow-Up	36
9.	Mortality Rates among Study Participants	37
10.	Distribution of cases according to the New York Heart Association (NYHA) functional classification at the last follow-up	38
11.	Distribution of age across phenotypes	40
12.	Distribution of sex across phenotypes	42
13.	Distribution of BMI across phenotypes	44
14.	Distribution of Alcohol and smoking across phenotypes	46
15.	Distribution of comorbidities across phenotypes	48
16.	Distribution of Cardiovascular Medications across Phenotypes: Analysis of ACEI, ARB, ARNI, SGLT2 Inhibitors, Diuretics, and MRA Usage across phenotypes	51
17.	Distribution of hospitalization due to heart failure during follow up across phenotypes	53
18.	Distribution of mortality across phenotypes	55
19.	Distribution of NYHA CLASS across phenotypes	57
20.	NYHA class of patients across different phenotypes (A, B and C) during last follow up visit	59

BABA FARID UNIVERSITY OF HEALTH SCIENCES
Sadiq Road, Faridkot-151203 (Pb.) INDIA
Phone No. 91-1639-256253 and Fax No. 91-1639-256234
Website: www.bfuhs.ac.in, Email: bfuhspc@gmail.com
(BFUHS – UNIVERSITY LIBRARY- Coordinator APC)

11-BFUHS (LI-PC-134)24/1368 Dated: October 28, 2024

Plagiarism Verification Certificate

Title of the thesis: **To Study Different Clinical Phenotypes And Short Term Follow Up In Patients Presenting With Heart Failure With Preserved Ejection Fraction.**

Total Page: **93 (Ninety Three only) eFSPC (eFile Sent for Plagiarism Check)**

Researcher: **Bhoj Raj Sharma**

Supervisor: **Dr. Gurpreet Singh Wander**

Research Centre: **Dayanand Medical College & Hospital, Ludhiana**

This is to report that the above thesis was scanned for similarity detection. Process and outcome is given below:

DID:	**2447318**	Software used:	**DRILLBIT**
Date:	**October 28, 2024**	Similarity Index:	**5% (Below 10 Percent)**

Total words count: **16484 (eFSPC)**

The complete report is submitted for review by the Supervisor and Co-Supervisor.

University Coordinator/
Name & Signature (Checked by)
(From University library)

The complete report of the above thesis has been reviewed by the undersigned. (Check Box)

☐ The similarity index is below accepted norms.

☐ The similarity index is above accepted norms, because of the following reasons:

1.....
2.....
3…….....
4…….....
5……

The thesis may be considered for the award of degree. (Relevant documents attached).

Research Scholar **Co-Supervisor** **Supervisor**

INTRODUCTION

The diagnosis and management of heart failure (HF) with preserved ejection fraction (HFpEF) is one of the most difficult tasks for clinicians today. Because of its increasing prevalence, it has been classified as an epidemic. Recent studies have shown that the same description can encompass distinct pathophysiological features. Hypertension, atrial fibrillation (AF), metabolic syndrome, ischemic coronary disease, valvulopathies, cardiomyopathies, and the cardiotoxic effects of medications and toxins are some of the most frequent reasons why HFpEF occurs. [1] Regarding organ damage, HFpEF is believed to be a benign condition. There has been little progress in discovering an effective treatment of HFpEF patients. Although those with HFpEF are thought to have a mild condition their symptoms, and signs, they have similar quality of life as compared to heart failure with reduced ejection fraction (HFrEF).[2]

Dr. Luchi et al. coined the term "HFpEF" in 1982 when They discovered common heart failure symptoms in a group of patients with preserved left ventricular (LV) ejection fraction (EF) for the first time.[3]

The European Society of Cardiology (ESC) recently referred patients with HFpEF to those with preserved LVEF ≥50% but structural heart disease or diastolic dysfunction, elevated plasma natriuretic peptide (NP) levels, and classic heart failure signs and symptoms. The exact cause of HFpEF is complex but Numerous elements have been implicated, including microvascular lesions, low-grade systemic inflammation, and general oxidative stress that developed in the context of endothelial dysfunction-related comorbidities, resulting in myocardial remodeling and fibrosis.[4]

The definition of this disease is the first step toward addressing the challenges associated with HF. There is no clear agreement on whether hemodynamic features or clinical state should be prioritized in the definition of heart failure. Comorbidities significantly influence patients' clinical presentation, course, and therapy with HFpEF.

Prevalence and Demographics:

It is estimated that between 1.5% and 5.5% of the general population has heart failure. It is believed that between 19% and 55% of all HF patients have HFpEF.[5] Over three decades of follow-up, the proportion of patients with HFpEF increased from 41% in 1985–1994 to 56% in 2005–2014, as stated by the Framingham study's authors. As per the registry data like Trivandrum Heart Failure Registry[6] and ASIAN-HF[7] the proportion of HFpEF in our country is approximately 19–25%, which is much lower as compared to that of the Western population. There is a possibility that many cases go undiagnosed in developing countries like India. The mean age of presentation of patients from India was around 58–68 years, which is about 10 years younger than the data reported from the west. The elderly have the highest rate of HFpEF, which is not surprising given the pathophysiological pathways. According to the statistics currently available, over 70% of patients with HFpEF are older than 65. However, the proportion of patients with HFpEF is only 40% when examining those under 65. Age-based analysis, [6] found that Women are more affected by HFpEF than men are. This implies that the disease's start and course may be influenced by a person's gender.

Etiology

Anemia, AF, respiratory conditions (chronic obstructive pulmonary disease and sleep-disordered breathing), kidney disease, and metabolic syndrome or its constituents (obesity, diabetes mellitus, hypertension) are among the conditions that are frequently associated with HFpEF.[7] According to recent studies, excessive adipose tissue accumulation at the epicardial level is a risk factor for HFpEF. This finding is predicated on the correlation between structural heart disease, excess epicardial fat, diastolic dysfunction, and atrial dilatation—all of which are believed to be prevalent in individuals with HFpEF.[8]

One crucial element of the pathophysiological process of HFpEF was suggested to be an inflammatory state. This results from changes in metabolism caused by diabetes, obesity, and high blood pressure.

Increased inflammation from these conditions leads to alterations in the metabolism of cardiomyocytes, coronary microvascular dysfunction, and ultimately subendocardial ischemia. Tumor necrosis factor-alpha (TNF-alpha) and transforming growth factor-beta 1 (TGF-beta1) have been shown to both cause and maintain this low-grade systemic inflammation.[9]

The Role of Biomarkers in Defining Heart Failure

Overall, there is a reasonable correlation between NT-proBNP and plasma BNP values, which can be used for patient diagnosis and follow-up.[10] It's also crucial to employ distinct cutoff values for various patient types. AF, Aging, obesity, pulmonary embolism, and chronic kidney disease are among the conditions that affect NP levels.[11]

Pathophysiology of HFpEF:

1. Left Ventricular Structure

The earliest model for HFpEF that was put forth in descriptive research depicted concentric left ventricular hypertrophy. All HFpEF patients were not adequately represented by this model.[12] Furthermore, a small minority of patients—up to 16%—have eccentric hypertrophy. Given that aging is one of the primary causes of HFpEF, left ventricular hypertrophy may occur but is not always linked to the condition.[13]

2. Left Ventricular Diastolic Dysfunction

Diastolic dysfunction is commonly defined as the left ventricle's failure to fill the end-diastolic volume (EDV) at low (but normal) pressure to a level suitable for the body's requirements. Although HFpEF was formerly known as diastolic dysfunction in heart failure, diastolic impairment is not superimposed by HFpEF. Diastolic dysfunction is recognized as a typical feature of human aging. This process is evident in the delay of active ventricular relaxation and the fibrosis of the LV walls, which causes the ventricular elasticity to decrease, as both sexes age.[14]

3. Atrial Dysfunction and AF

AF is more common in patients with HFpEF than in those with HFrEF. Research has demonstrated that in comparison to healthy individuals, patients with HFpEF require increased left atrial contraction to achieve

normal left ventricular filling even at an early stage.[15] Atrial contraction becomes increasingly important in preserving appropriate left ventricular filling as one ages. Atrial hypertrophy, a risk factor for AF, is ultimately brought on by prolonged atrial contraction, which also increases atrial pressure.Elevated pulmonary artery (PA) pressures, dilatation, and functional changes in the right cavity are indicators of hemodynamic suffering in the right heart in patients with HFpEF who suffer from AF, according to Melenovsky et al. [16]

4. Vascular Stiffness and Endothelial Dysfunction

HFpEF patients tend to have a poorer prognosis and lower quality of life due to the prevalence of endothelial dysfunction. Endothelial dysfunction is caused by a decrease in available nitric oxide (NO), which is produced by endothelial nitric oxide synthase (eNOS) or nitric oxide synthase 3 (NOS3) within endothelial cells. This hurts the production of cGMP as well as the activity of protein kinase CGMP-dependent 1 (PRKG1) and titin phosphorylation, which ultimately causes the cardiomyocytes to stiffen. Low-grade inflammation, which is often present in HFpEF patients, is thought to be the trigger that alters NOS3 activity in these patients.[17]

Researchers discovered that eating a diet high in fat and salt causes endothelial dysfunction, endothelial inflammation, and endothelial senescence, which in turn causes HFpEF by causing left atrial dilatation, diastolic dysfunction, left ventricular hypertrophy, and interstitial fibrosis.[18]

5. Chronotropic Reserve

HFpEF patients often experience chronotropic incompetence, which is the inability to increase heart rate. The prevalence of this condition varies between 57% and 77%, according to the study. This inability to elevate heart rate during exercise leads to an inadequate increase in cardiac output, contributing to the restrictions on exercise capacity seen in individuals with HFpEF.[19]

6. Cardiac Aging

The aging population is a significant factor contributing to the epidemic of HFpEF patients, as indicated by various studies. Diastolic dysfunction development is intimately linked to this mechanism. Aging results in several changes, including diastolic dysfunction, chronotropic incompetence, endothelial dysfunction, and vascular stiffening.

7. Inflammation and obesity

Inflammation and obesity may work together to cause cardiac senescence and the development of HFpEF.[20] Nutritional excess directly causes inflammation. Inflammation in cardiomyocytes, endothelial cells, and macrophages can be directly caused by nutrient overload. "Metabolic reprogramming" seems to refer to the basis for the induction of inflammation. Heart macrophages often contribute to homeostasis by eliminating dead, senescent cells and protecting the body from infections without triggering an immune reaction. The overabundance of nutrients induces metabolic reprogramming in macrophages, This results in inflammation promotion and negative consequences on the heart. Inflammation gets worse and the onset of a vicious cycle results in endothelial senescence and ultimately leads to endothelial dysfunction. [21]

8. Hypervolemia

The existence of volume overload in HFpEF patients is a topic of considerable debate. Clinically, symptoms such as edema, ascites, and pleural effusions are typically absent in HFpEF. However, there is a consensus that decompensation can occur in HFpEF due to congestion and volume overload, with the kidneys likely playing a significant role in this process. Patients with HFpEF often experience a chronic cardio-renal state that affects sodium and water balance.[22] In patients with HFrEF, cardiac decompensation leads to increased fluid in the arteries. In contrast, in HFpEF patients, this decompensation results in increased fluid in the interstitial spaces without a notable rise in blood volume. This difference helps explain why individuals with HFpEF do not respond as effectively to diuretics, while sodium-glucose co-transporter 2 inhibitors (SGLT2i) tend to have a more favorable

impact on dyspnea and reduced cardiac decompensation. It is crucial to use the terms “congestion” and “volume overload” carefully, as Even without a volume overload, congestion can happen. [23]

Phenotypes of HFpEF

Aging Phenotype:

Two of the main risk factors for HFpEF are age and hypertension. Studies have shown that HFpEF is highly prevalent in the elderly and very elderly (those who are 80 years of age or beyond).[24] Age-related alterations include a proinflammatory state and neurohormonal dysregulation. Age-related increases in arterial stiffness lead to systolic hypertension and expansion of the pulse pressure, which is the main consequence of aging on the vasculature. Collagen breakdown, cross-linking, and glycation are mediated by neuroendocrine activation (angiotensin II, aldosterone, and endothelin), metabolic changes (insulin, hyperglycemia, and advanced glycation products), and inflammation (cytokines, oxidative stress, and nuclear factor kappa B), which increase peripheral arterial resistance. Therefore, a significant factor influencing HFpEF is the age-related increase in arterial stiffness.[25]

Obesity phenotype:

Urban HFpEF registries in North America have identified a unique subset of HFpEF patients. The subgroup consists of obese and hypertensive African American women who are, on average, 10 to 15 years younger than their mainstream counterparts when diagnosed with HFpEF. An increased body mass index (BMI; kg/m2) has been identified as a risk factor for HFpEF. LVH and early LV diastolic dysfunction have been linked to obesity.[26] In addition to age and high blood pressure, central obesity in particular is a significant factor in arterial stiffness.[27] Regarding obesity in HFpEF, there are two noteworthy findings: (1) In women but not in males, obesity is correlated with arterial stiffness. (2)The duration of morbid obesity affects the LV response to weight loss.[28] Obesity is linked to a 4-fold higher prevalence of OSA, which increases arterial stiffness and contributes in multiple ways to the pathogenesis of HFpEF.Hypoxia

causes atrial and ventricular arrhythmias, oxidative stress triggers inflammation, and sympathetic activation raises left ventricular afterload.BMI and Unfavorable clinical outcomes were linked among the 4109 participants of the I-PRESERVE experiment, with the highest and lowest BMI categories having the highest rate of bad outcomes. In conclusion, central obesity seems to accelerate the development of HFpEF. [29]

CAD (Coronary Artery Disease) phenotype:

Obstructive CAD has not got as much attention in HFpEF as it has in HFrEF. In HFpEF registries, the prevalence of CAD varies from 35 percent to 53 percent. It should come as no surprise that individuals with both HFpEF and CAD had a worse prognosis and more LV function degradation than those with HFpEF alone.[30] Patients with HFpEF and angina face a much greater risk of mortality, myocardial infarction, coronary revascularization, and stroke than people without angina. In conclusion, the management and course of HFpEF are significantly impacted by the presence of CAD.[31]

Clinical Manifestations:

Patients often identify dyspnea as the primary condition that decreases their ability to exercise. Dyspnea can vary in severity and may occur at rest, during physical activity, or as paroxysmal nocturnal dyspnea. Additional symptoms include low exercise tolerance, extreme fatigue, and chest pain. Patients with HFpEF typically do not display clinical signs of right ventricular dysfunction, such as jugular venous distension and ankle edema. The clinical symptoms of HFpEF and HFrEF are identical, with no differences in how symptoms present based on the type of heart failure. However, diagnosing HFpEF is significantly more challenging because the ejection fraction remains normal. Because of this, it is challenging to differentiate between patients with HFpEF and those who are not suffering from cardiac dyspnea. [32]

Role of Echocardiography.

Transthoracic Echocardiography

The main parameter that allows classifying patients into one of the forms of HF, according to the ESC guidelines, is LVEF. The following parameters are more frequently evaluated: peak acceleration rate of mitral E velocity, ventricular filling velocity ratio (E/A), the ratio between rapid ventricular filling velocity and ventricular myocardial relaxation velocity (E/e'), isovolumic relaxation time (IVRT), peak tricuspid regurgitation (TR) velocity. The guideline recommendation is to use Left atrial volume in the assessment of diastolic dysfunction, the limit value being 34 mL/m^2.[33]

Differential Diagnosis

Respiratory disorders-pulmonary hypertension, chronic obstructive pulmonary disease (COPD).

Chronic kidney disease (CKD),

Anemia

Nephrotic syndrome

Hypothyroidism

Recent guidelines regarding the treatment of HFpEF

Pharmacological Therapy:

The effectiveness of drugs known to lessen symptom severity has not been demonstrated by research to date. Spironolactone improved both the functional and Outcomes related to the structural aspects of patients with HFpEF according to a meta-analysis of three randomized trials (TOPCAT, HOMAGE, and Aldo-DHF). However, when comparing HFpEF patients to HFrEF patients, spironolactone did not demonstrate a significant overall benefit in reducing all-cause mortality. Instead, it only reduced the rates of HF hospitalization. Given the positive outcomes observed in patients with HFrEF, valsartan/sacubitril (angiotensin receptor-neprilysin inhibitor, ARNI) emerged as a possible course of treatment for patients with HFpEF. However, the PARAGON-HF research did not demonstrate a statistically significant reduction in the Heart failure hospitalization rate decompensation or the risk of mortality from cardiovascular causes in patients with HFpEF.It has

been shown that thiazide diuretics such as chlorthalidone, which are used to treat hypertension, lessen the incidence of HFpEF in patients with hypertension. According to the ATTR-ACT study[34], tafamidis, a medication designed to treat transthyretin amyloid cardiomyopathy (ATTR-CM), can lower mortality and hospitalization rates if administered early in the course of the disease. These benefits are attributed to a decrease in heart contractile dysfunction. It is being investigated to provide myosin modulators for these HFpEF abnormalities. By binding to β-cardiac myosin, they either inhibit (mavacamten) or activate (omecamtiv mecarbil) cardiac contractility.

The development of SGLT2i, which function at the level of the proximal renal tubules and prevent glucose from being reabsorbed from the main urinary system while fostering natriuresis, marked a significant advancement in the treatment of these patients. These substances have demonstrated beneficial benefits on the pathological changes in heart failure and were developed to treat diabetes mellitus. Approximately 4.6mmHg of blood pressure reduction occurs.[35] A decrease in the interstitial fluid volume was seen more than the circulation volume, and This decrease was more apparent than the reduction achieved with diuretics. Reduction of arterial stiffness, a significant factor in the etiology of heart failure, is another effect of SGLT2i treatment. When SGLT2i is used, ketones are produced. This promotes the myocyte to use beta-hydroxybutyrate as an energy substrate instead of fatty acids, which maximizes myocardial oxygen consumption.**[36]** As a result of these mechanisms, the reduction in LV mass, reduction in parietal fibrosis, and improvement of diastolic function occurs. They have been proven to reduce the risk of both cardiovascular death and worsening episodes of heart failure in patients with HFrEF. The DELIVER study showed that dapagliflozin decreased the combined risk of worsening heart failure or cardiovascular death in patients with HFmrEF or HFpEF.[37] According to the EMPEROR-Preserved research, regardless of diabetes status, empagliflozin successfully lowers risks for patients with heart failure (HF) among patients of LVEF higher than 40%, including those with

mid-range (HFmrEF) and HFpEF. Both the ESC and the AHA/ACC guidelines now endorse the use of SGLT2i for managing HFpEF. These medications are thought to improve myocardial hypertrophy, fibrosis, diastolic dysfunction, and myocyte metabolism.[38]

Given the limited treatment options for HF, research is actively exploring new possibilities such as antioxidants, antifibrotic agents, anti-inflammatory drugs, and more. While the initial results are promising, further studies are essential.

Non-Pharmacological Therapy:

The non-pharmacological methods, similar to those used in HFrEF, aim to address the risk factors associated with heart failure. They promote a healthy Mediterranean-style diet that emphasizes low salt intake and a caloric intake suitable for optimizing body weight. In addition to this diet, regular physical exercise (150 minutes per week) and quitting smoking are strongly recommended. Regardless of the type of HF, AF is the most commonly encountered arrhythmia. This condition can result in worsening blood flow and reduced ability to exercise. Interatrial shunt procedures and devices are effective therapeutic options for the left atrial myopathy phenotype of HFpEF. Specifically, the transcatheter transvenous placement of an interatrial shunt device (IASD) can enhance hemodynamics during exercise, leading to improved functional capacity and a better quality of life.[39] Even after the best medical care has been administered, myocardial revascularization is advised for ischemic reasons in angina patients.

The diverse phenotypes of HFpEF and the lack of evidence-based treatments remain significant challenges in its management. As of right now, the strategy is largely tailored to each patient and primarily emphasizes phenotypes and comorbidities as presenting characteristics. Experts in cardiology suggested a particular treatment strategy and unique therapeutic response for traits that were commonly observed in the population. Thus, the present study was conducted to study different clinical phenotypes and their short-term follow-up in patients presenting with HFpEF. The goal of this narrative review is to present a nuanced understanding of HFpEF. The definition of HF is

thoroughly examined at the outset, and we made an effort to classify the patients based on biological and clinical traits known as phenotypes and to examine both the current treatment trends and their short-term follow-up.

AIM AND OBJECTIVE

1) To study different clinical phenotypes of patients with HFpEF.
2) To establish the correlation of studied clinical phenotypes with patient outcomes in HFpEF.

REVIEW OF LITERATURE

Heart failure is a diverse clinical illness that has been universally recognized and categorized. HF is currently divided into HF with reduced ejection fraction (HFrEF), mildly reduced EF (HFmrEF), and preserved EF (HFpEF), based on EF ≤40%, 41–49%, and ≥50%, respectively. Clinical research and treatment evidence in HFpEF is substantially limited compared to HFrEF, and this is reflected in the differences in the numbers of class I indications for these two entities in the most recent guidelines. Diagnosis of HFpEF is challenging; gaps in our understanding of the disease's pathophysiology, lack of universal diagnostic criteria, heterogeneity of HFpEF populations, and presence of multiple noncardiac comorbidities contribute to this. Although natriuretic peptide and imaging data generally confirm the diagnosis. Therefore, HFpEF is an entity that often remains underdiagnosed. This highlights how challenging it is to gather reliable data on HFpEF.

Peirre-Jean et al in 2024[40] studied that Patients presenting with symptoms of HFpEF are not a homogenous population. Different phenotypes can differ in prognosis and optimal management strategies. This study identified phenotypes of HFpEF by using the medical information database from a large university hospital center using machine learning. They explored the use of clinical variables from electronic health records in addition to echocardiography to identify different phenotypes of patients with HFpEF. The methodology identifies four phenotype clusters based on both clinical and echocardiographic characteristics, which have differing prognoses (death and cardiovascular hospitalization). This work demonstrated that artificial intelligence-derived phenotype could be used as a tool for physicians to assess risk and to target therapies that improve outcomes.

Xu et al in 2023[41] screened 189 patients in China with HFpEF who met the inclusion criteria and stratified them according to clinical characteristics, routine blood and biochemical parameters,

echocardiography, and comorbidities. Four HFpEF phenotypes were identified: phenotype 1 was a young patient with poor cardiac function but preserved renal function; phenotype 2 was an older male patient with cardiac and renal insufficiency; phenotype 3 had preserved LA morphology and function, and all patients in this group had higher ejection fractions than the other three groups; phenotype 4 was an older female patient with preserved cardiac function but poor renal function. According to the Cox proportional risk analysis, phenotype 2 patients had the highest risk of all-cause death (HR = 4.6094; 95% CI: 2.0373, 10.4291), and the Kaplan-Meier survival analysis revealed that their survival rates were significantly lower than those of the other three groups. Age and renal function should be the main emphasis of HFpEF patient staging and treatment, as analysis showed that these two parameters were critical in determining prognosis.

Anker et al in 2023[42] studied that HFpEF represents a highly heterogeneous clinical syndrome affected in its development and progression by many comorbidities. The left ventricular diastolic dysfunction may be a manifestation of various combinations of cardiovascular, metabolic, pulmonary, renal, and geriatric conditions. Thus, in addition to treatment with SGLT2i in all patients, the most effective method of improving clinical outcomes may be therapy tailored to each patient's clinical profile. To better outline a phenotype-based approach for the treatment of HFpEF, in this joint position paper, the Heart Failure Association of the European Society of Cardiology, the European Heart Rhythm Association, and the European Hypertension Society have developed an algorithm to identify the most common HFpEF phenotypes and identify the evidence-based treatment strategy for each, while taking into account the complexities of multiple comorbidities and polypharmacy.

Nyungen et al in 2021[43] studied that HFpEF is a rising health problem with heterogeneous presentation and no evidence-based treatment. An observational study on 477 patients diagnosed with HFpEF from seven hospitals in Southern Vietnam from January 2019 to December 2019 was conducted in Vietnam. Mean age was 67.6 (40.9% < 65 years).

The median ejection fraction was 63%. Valvular heart disease (VHD) was the leading cause of heart failure (35.9%). 78.6% had at least two comorbidities, mostly hypertension (68.6%).

Older patients (≥65 years) were more likely to be females (OR = 1.52); and had multimorbid conditions (OR = 3.14), including hypertension (OR = 4.28), diabetes (OR = 1.73), coronary artery disease (CAD) (OR = 2.50), dyslipidemia (OR = 1.94), and chronic kidney disease (OR = 2.44); and were more frequently prescribed statin (OR = 3.15). Younger individuals (<65 years) were associated with higher mineralocorticoid antagonist uptake (OR = 0.52) and VHD (OR = 0,40). Prescription rates for renin-angiotensin-aldosterone system inhibitor, beta blocker, mineralocorticoid antagonist, and loop diuretic were 72.5%, 59.1%, 43.0%, and 60.6%, respectively. Four phenotypes were identified, including the lean/elderly/multimorbid; congestive/metabolic; CAD-induced; and younger/(AF)/VHD. The novel phenotype "younger/AF/VHD" exhibited high symptom burden and poor functional capacity despite being the youngest and least multimorbid. The "lean/elderly/multimorbid" phenotype demonstrated the highest symptom severity and in-hospital mortality.

A cross-sectional study was conducted by Mitic et al., 2023[44] on 75 patients with HFpEF. An agglomerative hierarchical clustering was performed using the concentrations of cardiac remodeling biomarkers, BNP, and cystatin C. According to the obtained heat map of this analysis, we concluded two distinctive biomarker phenotypes within the HFpEF. The "remodeled phenotype" presented with significantly higher concentrations of cardiac remodeling biomarkers and cystatin C ($p < 0.001$), higher prevalence of myocardial infarction ($p = 0.047$), STEMI ($p = 0.045$), AF ($p = 0.047$), and anemia: lower erythrocytes count ($p = 0.037$), hemoglobin concentration ($p = 0.034$), and hematocrit ($p = 0.046$), compared to "non-remodeled phenotype." Echocardiography showed that patients within "remodeled phenotype" had significantly increased parameters of left ventricular remodeling: left ventricular mass index ($p < 0.001$), left ventricular mass ($p = 0.001$), diameters of the interventricular septum ($p = 0.027$), posterior wall ($p = 0.003$), and

function alterations, intermediate pauses duration >2.0 s ($p < 0.006$). Unsupervised hierarchical clustering applied to plasma concentration of various biomarkers in patients with HFpEF enables the identification of two biomarker phenotypes, significantly different in clinical characteristics and cardiac structure and function, whereas one phenotype particularly relates to patients with reduced ejection fraction. These findings imply distinct underlying pathophysiology within a unique cohort of HFpEF.

Fragasso et al in 2023[45] emphasized that HFpEF is frequently observed in elderly physically deconditioned subjects, mainly women with hypertension, obesity, glucose intolerance/diabetes, AF, anemia, coronary artery disease, chronic pulmonary disease, and chronic renal insufficiency. In practice, these conditions represent the majority of cardiac diseases we deal with in our daily clinical practice. For this reason, the HFpEF disease does not exist as a single entity and, as such, no specific unifying therapy could be found. New classification attempts still do not consider the multifaceted aspect of the HF syndrome and appear rather as an artefactual attempt to categorize a condition that is indeed not categorizable. The article aimed to critically review the construction of the concept of HFpEF syndrome and propose the return of a pathophysiological approach in the evaluation and treatment of patients. Considering the huge economic efforts employed up to date to run awfully expensive trials and research in this field, it is time to call action and redirect such resources towards more specific pathophysiological classifications and potential therapeutic targets.

A retrospective, observational study conducted by Shariff et al[46] in 2023 showed that there is sparsity in regional data surrounding HFpEF-related acute decompensated heart failure (ADHF) admissions in southeast Asia. This study aims to study the characteristics, clinical parameters, and outcomes related to HFpEF-linked ADHF admissions. A retrospective, observational study was conducted in a major cardiac tertiary center in Malaysia over 10 years (2009–2018). A total of 4,198 patients were identified, of which 632 had HFpEF. HFpEF

patients were significantly older (mean 67.6 years) and female (52.2%). A high proportion of HFpEF patients had hypertension (73.4%), diabetes (58.1%), coronary artery disease (57.9%), and ischaemic cardiomyopathy (50.8%), although this remains significantly lower versus non-HFpEF patients. AF was more common among HFpEF patients (34.7%). HFpEF patients in the study population appeared relatively stable, compared to nonHFpEF patients, supported by better blood results on admission, shorter duration of inpatient stay, lower use of emergency cardiac procedures, lower in-hospital mortality rates, and lower rates of HF readmissions and all-cause mortality. The present study highlights key characteristics of HFpEF patients in Malaysia and challenges the notion of the five major phenotypes of HF proposed by previous studies. Therefore, granularity in data collection and analysis is key, especially in a heterogeneous condition like HFpEF, and efforts should be improved to obtain more information on local HFpEF patients.

A review article by Tah et al., 2023[47] summarized that HFpEF is a clinical syndrome where patients exhibit signs and symptoms of heart failure due to elevated LV filling pressure, despite having a normal or nearly normal LV ejection fraction. HFpEF is more prevalent than HFrEF, and its diagnosis and treatment present greater challenges. While hypertension is the primary risk factor, other contributors such as obesity, diabetes, chronic renal disease, AF, and coronary artery disease play significant roles in the development of HFpEF.

This review summarized the current understanding of HFpEF, focusing on its pathophysiology, clinical presentation, diagnostic challenges, and both current and emerging treatments. Staying updated on the latest treatments for HFpEF is crucial to ensure that patients receive the best possible care.

Promising management strategies for HFpEF include the use of GnRH agonists, infusion of Apo A-I nanoparticles, low-level transcutaneous vagal stimulation (LLTS), and estrogen therapy in postmenopausal women. However, as of now, there is no proven curative treatment for HFpEF.

HFpEF is a multi-organ, systemic syndrome that involves multiple cardiac and extracardiac pathophysiologic abnormalities. Because HFpEF is a heterogeneous syndrome and resistant to a “one-size-fits-all” approach it has proven to be very difficult to treat. For this reason, several research groups have been working on methods for classifying HFpEF and testing targeted therapeutics for the HFpEF subtypes identified. Apart from conventional classification strategies based on comorbidity, etiology, left ventricular remodeling, and hemodynamic subtypes, researchers have been combining deep phenotyping with innovative analytical strategies (e.g., machine learning) to classify HFpEF into therapeutically homogeneous subtypes over the past few years. Despite the growing excitement for such approaches, there are several potential pitfalls to their use, and there is a pressing need to follow up on data-driven HFpEF subtypes to determine their underlying mechanisms and molecular basis. Heinzel and Shah in2022[48] provided a framework for understanding the phenotype-based approach to HFpEF by reviewing (1) the historical context of HFpEF; (2) the current HFpEF paradigm of comorbidity-induced inflammation and endothelial dysfunction; (3) various methods of sub-phenotyping HFpEF; (4) comorbidity-based classification and treatment of HFpEF; (5) machine learning approaches to classifying HFpEF; (6) examples from HFpEF clinical trials; and (7) the future of phenomapping (machine learning and other advanced analytics) for the classification of HFpEF.

Reddy et al in 2022[49] conducted a retrospective case-control study to evaluate H2FPEF and HFA-PEFF scores and a PCWP/cardiac output (CO) slope of more than 2 mm Hg/L/min to diagnose HFpEF. This retrospective case-control study included patients with unexplained dyspnea from 6 centers in the US, the Netherlands, Denmark, and Australia from March 2016 to October 2020. Diagnosis of HFpEF (cases) was definitively ascertained by the presence of elevated PCWP during exertion; control individuals were those with normal rest and exercise hemodynamics. Among 736 patients, 563 (76%) were diagnosed with HFpEF (mean [SD] age, 69 [11] years; 334 [59%]

female) and 173 (24%) represented controls (mean [SD] age, 60 [15] years; 109 [63%] female). H2FPEF and HFA-PEFF Scores differentiated patients with HFpEF from controls, but the H2FPEF score displayed a greater area under the curve. (0.845; 95% CI, 0.810-0.875) compared with the HFA-PEFF score (0.710; 95% CI, 0.659-0.756) (difference, −0.134; 95% CI, –0.177 to −0.094; P < .001). Both scores showed robust specificity, but sensitivity was lower for HFA-PEFF, with a false-negative rate of 55% for low probability scores, compared to 25% for the H2FPEF score. Use of the PCWP/CO slope to redefine HFpEF rather than exercise PCWP reclassified 20% (117 of 583) of patients, but patients reclassified from HFpEF to control by this metric had clinical, echocardiographic, and hemodynamic features typical of HFpEF, including elevated resting PCWP in 66% (46 of 70) of reclassified patients.

Gulea et al in 2021[50] identified Patients with COPD and HF in the U.S. administrative claims database OptumLabs DataWarehouse between 2008 and 2018. All-cause and cause-specific (HF) hospitalization, acute exacerbation of COPD (AECOPD, severe and moderate combined), mortality, and healthcare resource use were compared between HF phenotypes. From 5,419 patients with COPD, 70% had HFpEF, 20% had HFrEF, and 10% had HFmEF. All-cause Hospitalization rates were similar across all groups.; however, patients with COPD and HFrEF had a greater risk of HF-specific hospitalization (hazard ratio [HR], 1.54; 95% confidence interval [CI], 1.29–1.84) and mortality (HR, 1.17; 95% CI, 1.03–1.33) than patients with COPD and HFpEF. Conversely, patients with COPD and HFrEF had a lower risk of AECOPD than those with COPD and HFpEF (HR, 0.75; 95% CI, 0.66–0.87). The rates of long-term stays in skilled nursing facilities and emergency room visits were lower for individuals with COPD and HFrEF compared to those with COPD and HFpEF. Outcomes in patients with comorbid COPD and HFpEF are largely driven by COPD. Given the paucity of treatments for HFpEF, better differentiation between cardiac and respiratory symptoms may provide an opportunity to reduce the risk of AECOPD. Patients with both Chronic Obstructive

Pulmonary Disease (COPD) and HFrEF had the highest risk of heart failure-related death and hospitalization, highlighting the significance of optimizing HFrEF therapy as advised by guidelines for this population.

Cohen et al in 2020[51] conducted a latent class analysis among participants of the TOPCAT (Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist Trial) to identify HFpEF phenogroups based on standard clinical features. Additionally, we assessed differences in multiple biomarkers measured from frozen plasma. Evaluation of cardiac and arterial structure/function via echocardiography and arterial tonometry, prognosis, and response to spironolactone. Three distinct phenogroups of HFpEF were identified. Phenogroup 1 (n = 1,214) had a younger age, a higher prevalence of smoking preserved functional class, and the least evidence of LV hypertrophy and arterial stiffness. Phenogroup 2 (n = 1,329) was older and exhibited normotrophic concentric left ventricular remodeling, AF, left atrial enlargement, large artery stiffening, and elevated biomarkers of vascular calcification and innate immunity. Phenogroup 3 (n = 899) showed increased functional impairment, diabetes, obesity, chronic kidney disease, concentric left ventricular hypertrophy, elevated renin levels, and biomarkers indicating tumor necrosis factor-alpha–mediated inflammation, liver fibrosis, and tissue remodeling. In comparison to phenogroup 1, phenogroup 3 showed the highest risk for the primary outcome, which includes cardiovascular death, hospitalization due to heart failure, or aborted cardiac arrest. The hazard ratio (HR) for this group was 3.44, with a 95% confidence interval (CI) of 2.79 to 4.24. Additionally, phenogroups 2 and 3 exhibited similar rates of all-cause mortality, with phenogroup 2 having an HR of 2.36 (95% CI: 1.89 to 2.95) and phenogroup 3 an HR of 2.26 (95% CI: 1.77 to 2.87). Spironolactone randomized therapy led to a more significant reduction in the risk of the primary endpoint for phenogroup 3 (Hazard Ratio: 0.75; 95% Confidence Interval: 0.59 to 0.95; p-value for interaction = 0.016). Spironolactone randomized therapy led to a more significant reduction in the risk of the primary endpoint for phenogroup 3 (Hazard Ratio: 0.75; 95% Confidence Interval: 0.59 to 0.95; p-value

for interaction = 0.016). The results remained consistent even after excluding participants from Eastern Europe. ed to a more significant reduction in the risk of the primary endpoint for phenogroup 3 (Hazard Ratio: 0.75; 95% Confidence Interval: 0.59 to 0.95; p-value for interaction = 0.016).

Hedmen et al in 2019[52] utilized model-based clustering on 32 echocardiograms and 11 clinical and laboratory variables collected from 320 stable HFpEF outpatients in the Karolinska-Rennes cohort study (56% female, median age 78 years (IQR: 71–83). Baseline proteomics and the combined outcome of hospitalization for HF or all-cause death were used in secondary analyses. They identified six phenogroups with significant differences in the prevalence of concomitant AF, anemia, and kidney disease ($p<0.05$). Fifteen out of 86 plasma proteins showed significant differences between phenogroups (false discovery rate, FDR < 0.05), including biomarkers for heart failure, AF, and kidney function. The composite endpoint showed significant differences between phenogroups (log-rank $p<0.001$) across short-term (100 days), mid-term (18 months), and long-term follow-up (1000 days). Phenogroup 2 was older and had poorer diastolic and right ventricular function, along with a higher burden of risk factors, including AF (85%), hypertension (83%), and chronic obstructive pulmonary disease (30%).In this group, one-third experienced the primary outcome by 100 days, while two-thirds reached it by 18 months (HR (95% CI) compared to phenogroups 1, 3, 4, 5, and 6: 1.5 (0.8–2.9); 5.7 (2.6–12.8); 2.9 (1.5–5.6); 2.7 (1.6–4.6); 2.1 (1.2–3.9).

Shah et al in 2015[53] conducted thorough clinical, laboratory, ECG, and echocardiographic phenotyping of the 397 HFpEF patients they investigated. They employed several statistical learning algorithms, such as penalized model-based clustering and unbiased hierarchical cluster analysis of phenotypic data (67 continuous variables), to identify and describe mutually exclusive groups that comprise a unique categorization of HFpEF. All phenomapping analyses were performed by investigators blinded to clinical outcomes, and Cox regression was

used to demonstrate the clinical validity of phenomapping. The mean age was 65±12 years; 62% were female; 39% were black; and comorbidities were common. Although all patients met published criteria for the diagnosis of HFpEF, phenomapping analysis classified study participants into 3 separate groups that varied significantly in terms of invasive hemodynamics, cardiac structure and function, clinical features, and outcomes (eg, phenogroup 3 had an increased risk of HF hospitalization [hazard ratio, 4.2; 95% confidence interval, 2.0–9.1] even after conventional risk factors have been adjusted [*P*<0.001]). The HFpEF phenogroup classification, including its ability to stratify risk, was successfully replicated in a prospective validation cohort (n=107). Phenomapping results in a novel classification of HFpEF. Statistical learning algorithms applied to dense phenotypic data may allow improved classification of heterogeneous clinical syndromes, with the ultimate goal of defining therapeutically homogeneous patient subclasses.

Bhatia et al., 2006[54] studied 2802 patients admitted to 103 hospitals in the province of Ontario, Canada, with a discharge diagnosis of heart failure whose ejection fraction had also been assessed. The patients were grouped into three groups.: those with an ejection fraction of less than 40 percent HFrEF, those with an ejection fraction of 40 to 50 percent (HFmEF), and those with an ejection fraction of more than 50 percent (HFpEF). Thirty-one percent of the patients had an ejection fraction of more than 50 percent. Patients with heart failure and preserved ejection fraction tend to be older and female and to have a history of hypertension and AF. The presenting history and clinical examination findings were similar for the two groups. The mortality rates for patients with an ejection fraction over 50 percent were not significantly different from those for patients with an ejection fraction under 40 percent at 30 days. (5 percent vs. 7 percent, P=0.08) and at 1 year (22 percent vs. 26 percent, P=0.07); the adjusted one-year mortality rates were also not significantly different in the two groups (hazard ratio, 1.13; 95 percent confidence interval, 0.94 to 1.36; P=0.18). The rates of

readmission for heart failure and in-hospital complications did not differ between the two groups.

MATERIALS AND METHODS

SOURCE OF DATA

The present study included all the patients fulfilling the criteria of HFpEF who came to OPD and the emergency department of Hero DMC Heart Institute.

SAMPLE SIZE

The sample size was a total number of heart failure patients with preserved ejection fraction including outpatient and inpatients who presented at Hero DMC Heart Institute during the defined duration of the study.

INCLUSION CRITERIA:

Heart failure patients with preserved ejection fraction were defined as satisfying all three criteria:

(1) Age ≥ 18years

(2) EF ≥50%

Table 1: NT PRO BNP cut off

Acute Dyspnea	**To identify acute HF**	
	Single cut-off point	
	NT-proBNP	<900 pg/mL
	Multiple cut off point	
	NT-proBNP	<450 pg/mL for age <50 yr <900 pg/mL for age 50-75 yr < 1800 pg/mL for age > 75 yr
Outpatient Screening	**NT-proBNP**	<125 pg/mL for age <75 yr
		<450 pg/mL for age ≥75 yr

EXCLUSION CRITERIA:

The exclusion criteria included all those patients presenting with:

1. End-stage renal (creatinine clearance < 30ml/min by cock croft ---gault formula)
2. Severe hepatic impairment (Child-Pugh class B or C)
3. Prior documented EF <50%
4. Life expectancy <1 year due to noncardiac etiologies.

5. Pregnancy or lactation
6. Patients with uncontrolled blood pressure
7. Concurrent enrolment in any other trial
8. **METHOD OF COLLECTION OF DATA**

- **DATA COLLECTION:** Demographic features like age, presenting symptoms, medical and behavioral history, and functional status were obtained through direct interview and physical examination. Investigations, risk factors, and comorbidities were taken from medical records or newly identified, including coronary artery disease (CAD), hypertension (HTN), atrial fibrillation/atrial flutter (AF), diabetes mellitus (DM), chronic kidney failure (CKD), smoking, obesity, peripheral artery disease (PAD), cerebral vascular accident (CVA), obstructive pulmonary disease, and cancer.

All the heart failure patients diagnosed with preserved ejection fraction HFpEF according to our diagnostic criteria will be enrolled in the study.

Table 2: H_2FPEF Score

Clinical variable	Values	Points
Heavy	BMI >30kg/m2	2
Hypertensive	2 or more antihypertensives	1
Atrial fibrillation	Paroxysmal or persistant	3
Pulmonary hypertension	Pulmonary artery systolic pressure >35mmHg	1
Elderly	>60 years	1
Filling pressures	Doppler echocardiographic E/e' 9	1

Table 3: HFA-PEFF score

MAJOR	septal e <7cm/s or lateral e <10cm/s or average E/e >15 or TR velocity >2.8m/s(PASP >35mmHg)	LAVI >34ml/m2 Or LVMI >149/122g/m2 and RWT >0.42	NT proBNP >220pg/ml or BNP >80pg/ml	NT proBNP >660pg/ml or BNP >240pg/ml
MINOR	Average E/e 9-14 or GLS <16%	LAVI 29-34ml/m2 or LVMI >115/95g/m2 Or RWT >0.42 Or LV wall thickness >12mm	NT proBNP 125-220 pg/ml or BNP 35-80pg/ml	NT proBNP 365-660pg/ml or BNP 105-240pg/ml

Major criteria: 2 points

Minor criteria: 1 point

SCORE >5 =HFpEF

We divided patients into 3 different phenotypes.

Phenotype 1 (n = 39)) were mostly elderly lean females with the worst symptom severity and functional capacity and highest comorbid burden, especially HTN, DM, AF, and CKD.

Phenotype 2 (n= 99) consisted of mostly obese, females with significant dyslipidemia, HTN, CAD, and DM.

Phenotype 3 (n= 37) included young patients predominantly males, in which CAD was the main cause for HFpEF.

DURATION OF STUDY/NO. OF CASES

All patients fulfilling the criteria of HFpEF who came to OPD and emergency department of Hero DMC Heart Institute for 1.5 years and their follow-up for 6 months.

OUTCOME: Different clinical phenotypes of the patient presenting with HFpEF and their short-term outcome were studied in terms of repeat hospitalization in 6 months or mortality.

STATISTICAL ANALYSIS

Data were described in terms of range; mean ±standard deviation (± SD), frequencies (number of cases), and relative frequencies (percentages) as appropriate. Comparison of quantitative variables between the study groups was done using the Kruskal-Wallis Test with post hoc Tukey's. For comparing categorical data, the Chi-square ($\chi 2$) test was performed and the Fisher exact test was used when the expected frequency is less than 5. A probability value (p-value) less than 0.05 was considered statistically significant. All statistical calculations were done using (Statistical Package for the Social Science) SPSS 21.0 version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

OBSERVATION AND RESULTS

This single-center, prospective observational study was conducted in the Hero DMC Heart Institute Department of Cardiology. The sample size included patients with preserved ejection fraction (HFpEF) during the study period. We divided patients into 3 different phenotypes. Phenotype 1 (n = 39)) were mostly elderly lean females with the worst symptom severity and functional capacity and highest comorbid burden, especially HTN, DM, AF, and CKD. Phenotype 2 (n= 99) consisted of mostly obese, females with significant dyslipidemia, HTN, CAD, and DM. Phenotype 3 (n= 37) included young patients predominantly males, In which CAD was the main cause of HFpEF.

Table 4: Age distribution of the patients

AGE GROUP	No. of cases	%age
< 65	81	46.3
> 65	94	53.7
Total	175	100.0

Age distribution of the study patients shows that 46.3% of patients were less than 65 years old and 53.7% of patients were more than 65 years old given in table 4 and figure 1

Figure 1: Age distribution of the patients

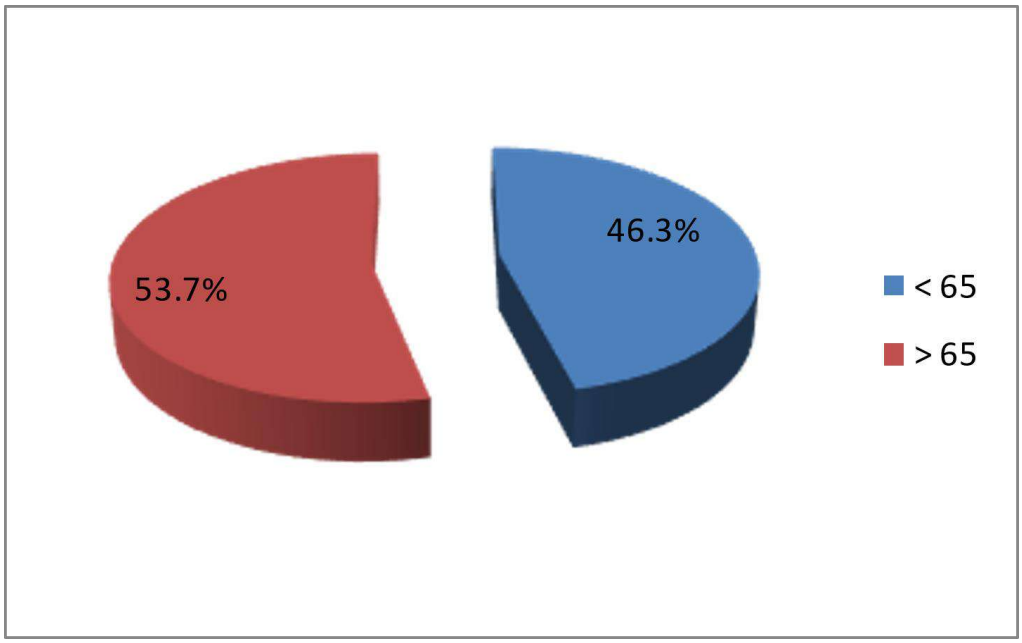


Table 5: Gender distribution of the patients

SEX	No. of cases	%age
F	115	65.7
M	60	34.3
Total	175	100.0

The gender distribution of the study population is shown in Table 5 and Figure 2 which shows that 65.7% of study patients are female and 34.3% of patients are male.

Figure 2: Gender distribution of the patients

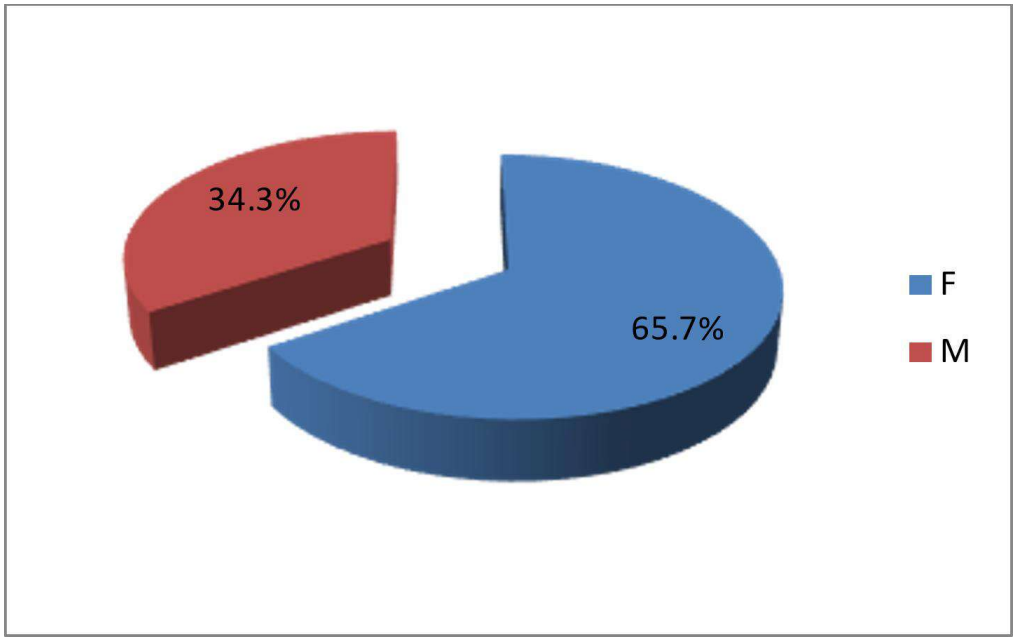


Table 6: BMI of patients enrolled

BMI GROUP	No. of cases	%age
< 18.5	4	2.3%
18.5-22.9	44	25.1%
23-24.9	43	24.6%
25-29.9	63	36.0%
> 30	21	12.0%
Total	175	100.0%

The distribution of the study population according to BMI is given in Table 6 and Figure 3

Figure 3: BMI of patients enrolled

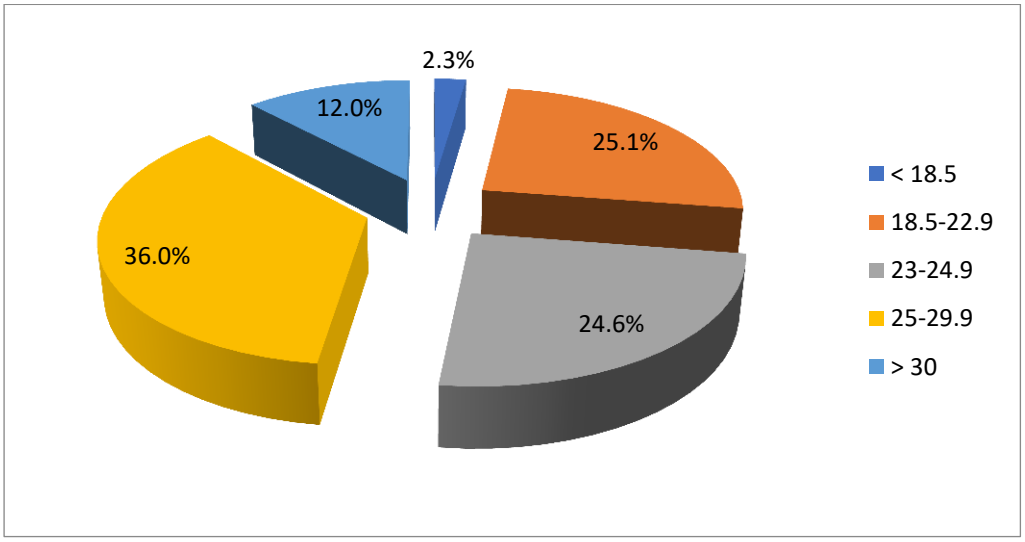


Table 7: Distribution of Cases by Risk Factors

Risk factors	No. of cases	%age
ALCOHOLIC	12	6.9
SMOKER	11	6.3

Figure 4: Distribution of Cases by Risk Factors

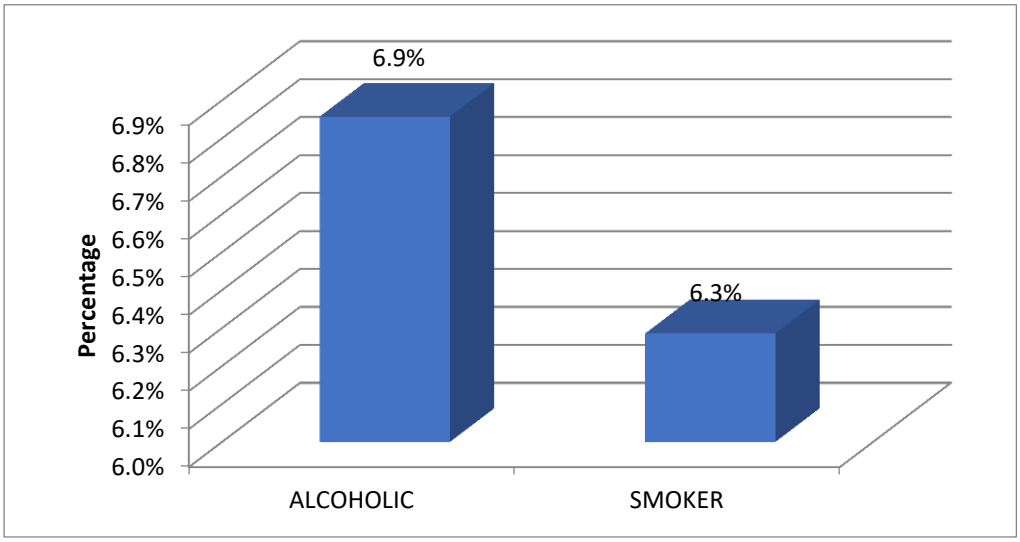
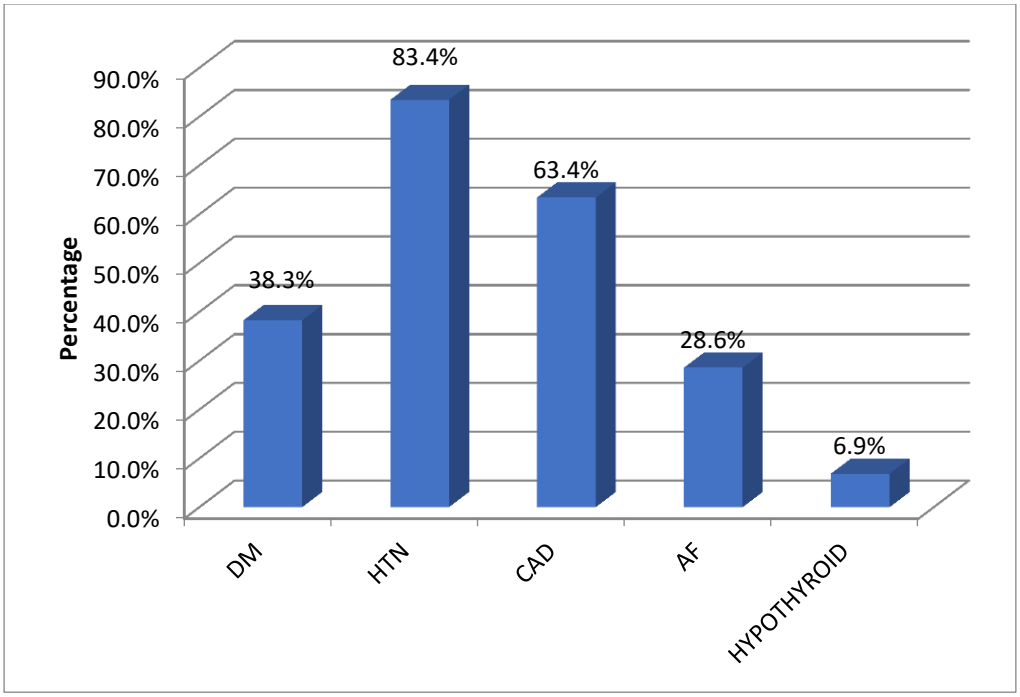


Table 8: Distribution of cases by comorbidities

Comorbidities.	No. of cases	%age
DM	67	38.3
HTN	146	83.4
CAD	111	63.4
AF	50	28.6
HYPOTHYROID	12	6.9

The comorbidity data reveals that hypertension (83.4%) is the most common condition, followed by coronary artery disease (63.4%) and diabetes mellitus (38.3%). AF (28.6%) while hypothyroidism (6.9%) is less frequent

Figure 5: Distribution of cases by comorbidities



.

Table 9: Distribution of Cases by Medication Class

	No. of cases	%age
ACEI	50	28.6
ARB	84	48.0
ARNI	16	9.1
SGLT2	47	26.9
DIURETICS	105	60.0
MRA	62	35.4

The data on medication usage reveals that diuretics (60.0%) are the most commonly used treatment, followed by angiotensin II receptor blockers (ARBs) (48.0%). Mineralocorticoid receptor antagonists (MRAs) are used in 35.4%, and angiotensin-converting enzyme inhibitors (ACEIs) in 28.6% of the cases. SGLT2 inhibitors are taken by 26.9%, while angiotensin receptor-neprilysin inhibitors (ARNIs) are used by 9.1%

Figure 6: Distribution of Cases by Medication Class

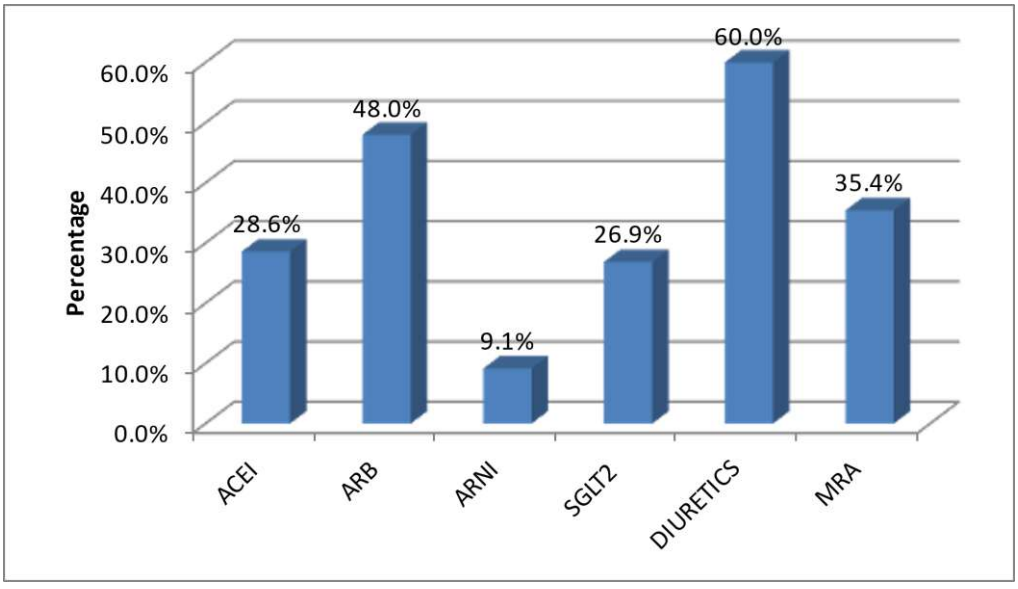


Table 10: Distribution of Cases by NYHA Classification

NYHA CLASS	No. of cases	%age
II	118	67.4
III	57	32.6
Total	175	100.0

The above table shows that out of 175 cases, 67.4% (118 individuals) were categorized as NYHA Class II Meanwhile, 32.6% (57 individuals) were in NYHA Class III,

Figure 7: Distribution of Cases by NYHA Classification

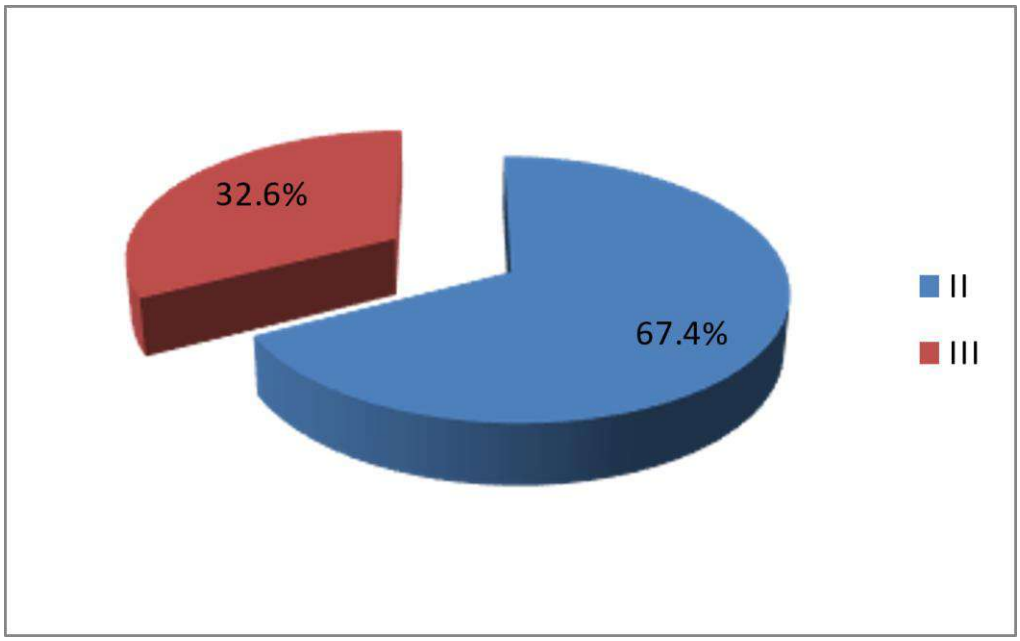


Table 11: Hospitalizations Due to Heart Failure During Follow-Up

No. of hospitalization due to heart failure during follow-up	No. of cases	%age
NO	126	72.0
YES	49	28.0
Total	175	100.0

During the follow-up period, 28.0% of patients (49 cases) were hospitalized due to heart failure, while the majority, 72.0% (126 cases), did not require hospitalization. This data highlights that heart failure continues to present a serious risk for almost one-third of the population.

Figure 8: Hospitalizations Due to Heart Failure during Follow-Up

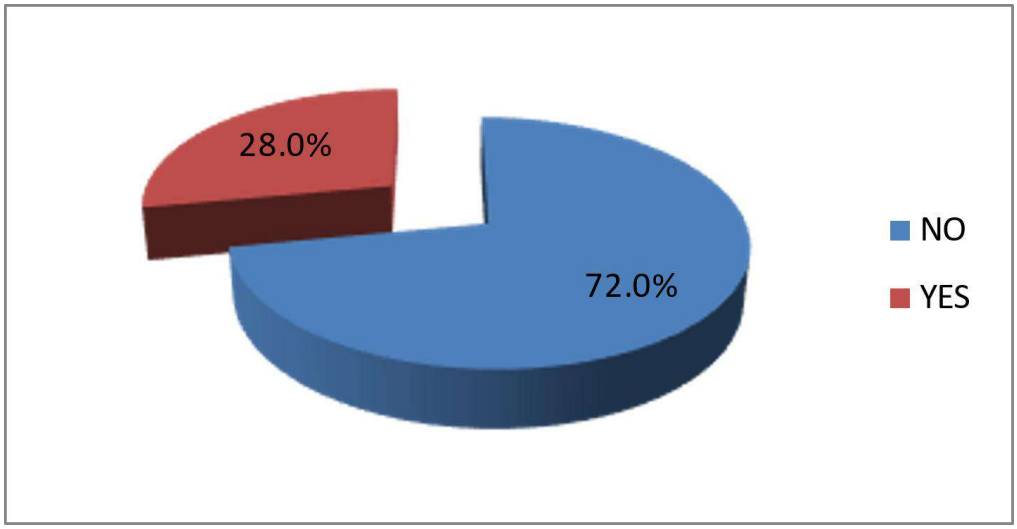


Table 12: Mortality Rates among Study Participants

Mortality	No. of cases	%age
NO	167	95.4
YES	8	4.6
Total	175	100.0

Out of 175 cases, only 8 individuals (4.6%) experienced mortality during the study period, while the majority, 167 individuals (95.4%), survived.

Figure 9: Mortality Rates among Study Participants

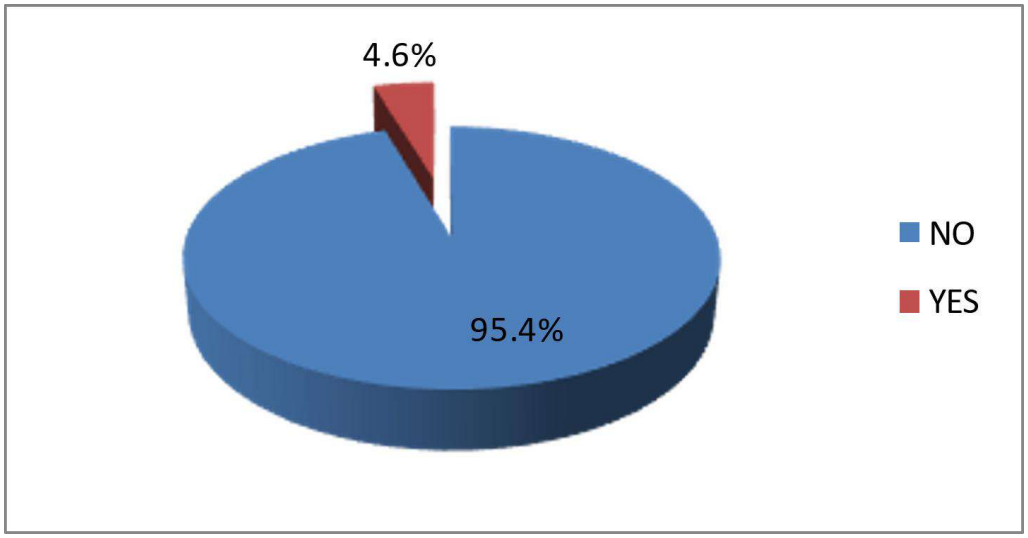


Table 13: Distribution of cases according to the New York Heart Association (NYHA) functional classification at the last follow-up

NYHA CLASS LAST FOLLOW UP	No. of cases	%age
I	33	18.9%
II	76	43.4%
III	63	36.0%
IV	3	1.7%

The above table shows that at the last follow-up 18.9% % of patients belonged to NYHA class 1,43.40 % of patients belonged to NYHA class II, 36.0% of patients belonged to NYHA class III and 1.7 % of patients were in class IV NYHA group

Figure 10: Distribution of cases according to the New York Heart Association (NYHA) functional classification at the last follow-up

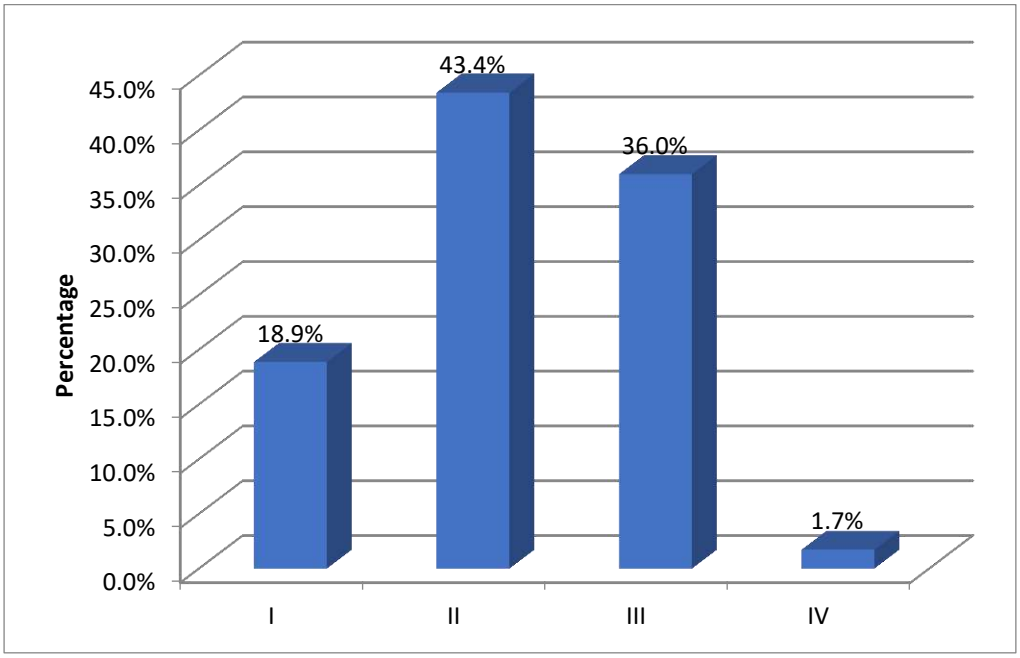


Table 14: Distribution of age across phenotypes

	PHENOTYPE	A		B		C		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
AGE GROUP	< 65	1	2.6	43	43.4	37	100.0	81	73.248	0.001
	> 65	38	97.4	56	56.6	0	0.0	94		
Total		39	100.0	99	100.0	37	100.0	175		

In the present study Phenotype A strongly associated with older age (97.4% of cases are >65 years), Phenotype B is more evenly distributed between age groups (56.6% >65 years, 43.4% <65 years), while Phenotype C exclusively appears in younger individuals (100% <65 years). The chi-square value of 73.248 and p-value of 0.001 indicates that the difference in age groups is statistically significant.

Figure 11: Distribution of age across phenotypes

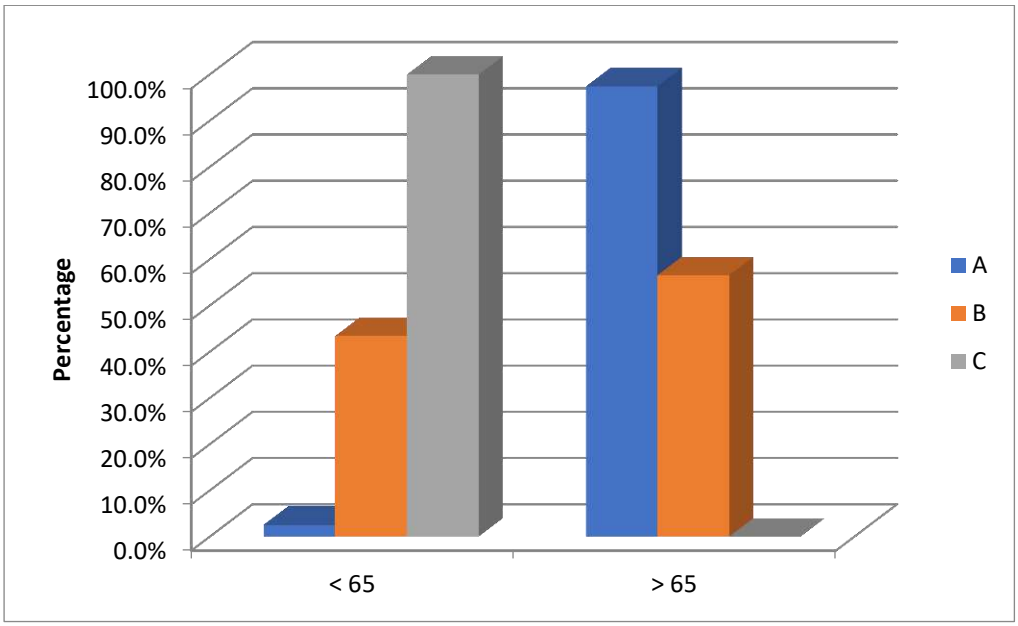


Table 15: Distribution of sex across phenotypes

	PHENOTYPE	A		B		C		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
SEX	F	22	56.4	85	85.9	8	21.6	115	51.256	0.001
	M	17	43.6	14	14.1	29	78.4	60		
Total		39	100.0	99	100.0	37	100.0	175		

Phenotype A shows a relatively balanced distribution between females (56.4%) and males (43.6%), Phenotype B demonstrates a strong female predominance (85.9% female vs 14.1% male), while Phenotype C shows a clear male predominance (78.4% male vs 21.6% female). The chi-square value of 51.256 with a p-value of 0.001 indicates these gender-based differences are statistically significant.

Figure 12: Distribution of sex across phenotypes

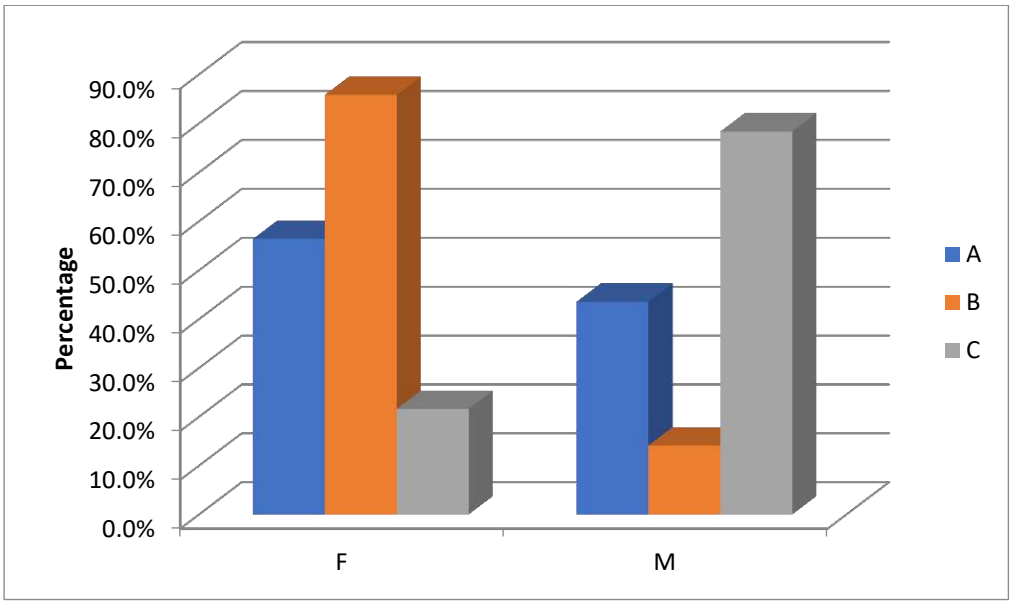


Table 16: Distribution of BMI across phenotypes

	PHENOTYPE	A		B		C		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
BMI GROUP	< 18.5	3	7.7%	1	1.0%	0	0.0%	4	41.756	0.001
	18.5-22.9	21	53.8%	14	14.1%	9	24.3%	44		
	23-24.9	9	23.1%	21	21.2%	13	35.1%	43		
	25-29.9	6	15.4%	45	45.5%	12	32.4%	63		
	> 30	0	0.0%	18	18.2%	3	8.1%	21		
Total		39	100.0%	99	100.0%	37	100.0%	175		

Phenotype A shows highest concentration in the normal BMI range (53.8% in 18.5-22.9), with no cases in obese category (>30); Phenotype B shows a notable presence in overweight (45.5%) and obese (18.2%) categories; Phenotype C shows more spread distribution across all BMI ranges with notable presence of overweight ranges (35.1% in 23-24.9 and 32.4% in 25-29.9), with no underweight cases. The chi-square value of 24.175 with a p-value of 0.001 indicates these BMI-based differences are statistically significant.

Figure 13: Distribution of BMI across phenotypes

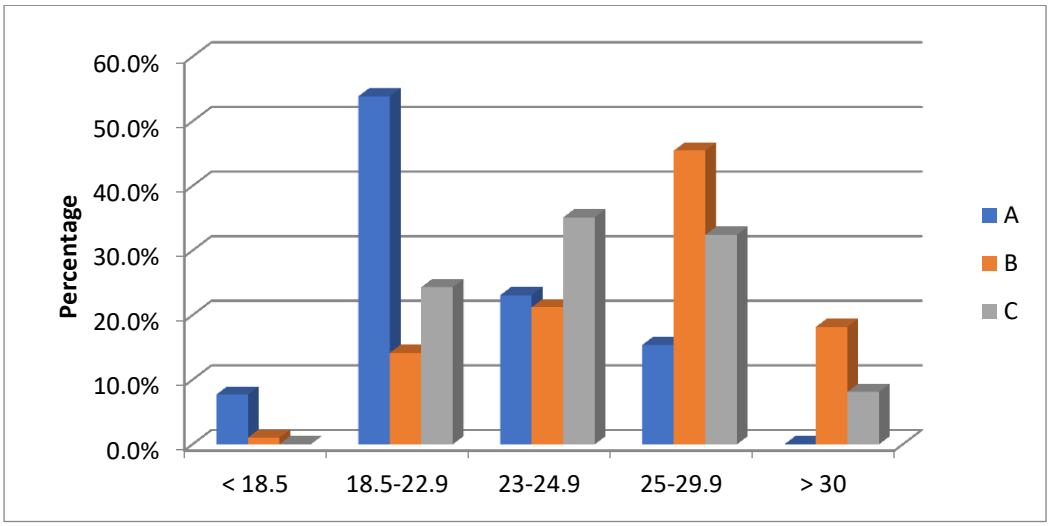


Table 17: Distribution of Alcohol and smoking across phenotypes

	PHENOTYPE	A		B		C		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
ALCOHOLIC	NO	38	97.4	89	89.9	36	97.3	163	3.756	0.153
	YES	1	2.6	10	10.1	1	2.7	12		
SMOKER	NO	37	94.9	92	92.9	35	94.6	164	0.241	0.887
	YES	2	5.1	7	7.1	2	5.4	11		
Total		39	100.0	99	100.0	37	100.0	175		

All phenotypes show low proportions of alcoholics: Phenotype A (2.6%), Phenotype B (10.1%), and Phenotype C (2.7%), with a chi-square value of 3.756 and p-value of 0.153. Similarly, for smoking, all phenotypes show low proportions of smokers: Phenotype A (5.1%), Phenotype B (7.1%), and Phenotype C (5.4%), with a chi-square value of 0.241 and p-value of 0.887. The high p-values (>0.05) for both lifestyle factors indicate that there are no statistically significant associations between phenotypes and alcohol consumption or smoking habits in the study population.

Figure 14: Distribution of Alcohol and smoking across phenotypes

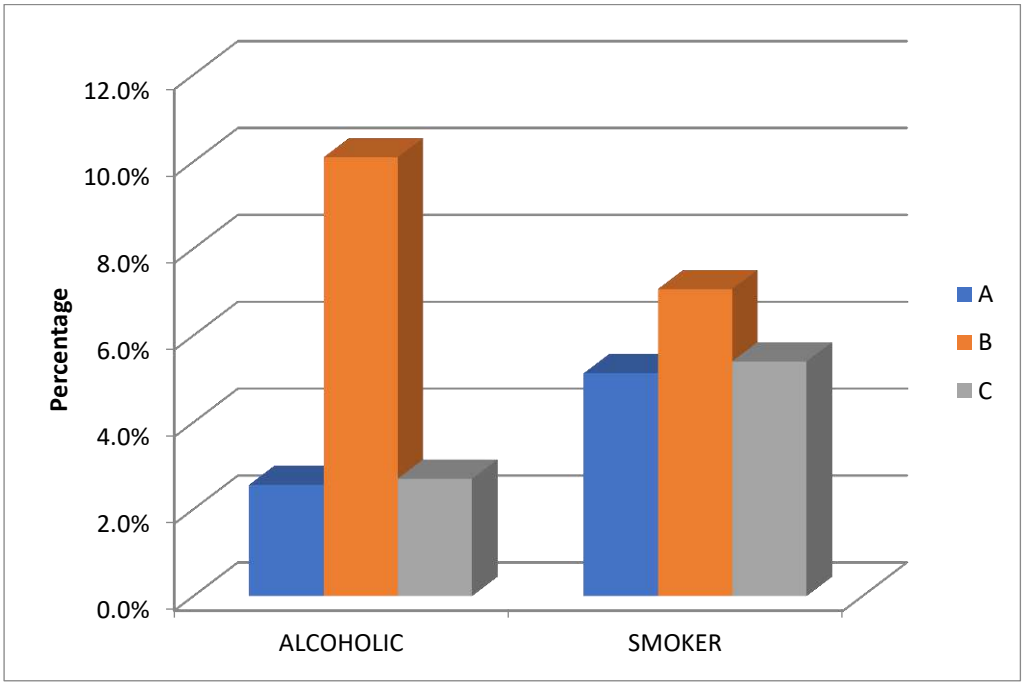


Table 18: Distribution of comorbidities across phenotypes

	PHENOTYPE	A		B		C		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
DM	NO	25	64.1	55	55.6	28	75.7	108	4.736	0.094
	YES	14	35.9	44	44.4	9	24.3	67		
HTN	NO	6	15.4	7	7.1	16	43.2	29	25.542	0.001
	YES	33	84.6	92	92.9	21	56.8	146		
CAD	NO	10	25.6	43	43.4	11	29.7	64	8.785	0.067
	YES	29	74.4	56	56.6	26	70.3	111		
AF	NO	24	61.5	74	74.7	27	73.0	125	2.470	0.294
	YES	15	38.5	25	25.3	10	27.0	50		
HYPOTHYROID	NO	38	97.4	89	89.9	36	97.3	163	3.756	0.153
	YES	1	2.6	10	10.1	1	2.7	12		
Total		39	100	99	100.	37	100.	175		

For DM, the distribution shows varying patterns: Phenotype A (35.9%), Phenotype B (44.4%), and Phenotype C (24.3%) with a chi-square value of 4.736 and p-value of 0.094, indicating no statistically significant association. However, for HTN, there's a significant variation: Phenotype A (84.6%), Phenotype B (92.9%), and Phenotype C (56.8%) with a chi-square value of 25.542 and p-value of 0.001, indicating a strong statistical association between phenotypes and hypertension, with Phenotypes A and B showing notably higher proportions of hypertensive cases compared to Phenotype C. Coronary Artery Disease (CAD) shows high prevalence across all phenotypes (A: 74.4%, B: 56.6%, C: 70.3%, p=0.067); AF varies among phenotypes (A: 38.5%, B: 25.3%, C: 27.0%, p=0.294); and hypothyroidism shows low prevalence (A: 2.6%, B: 10.1%, C: 2.7%, p=0.153). Notably, none of these conditions show statistically significant associations with phenotypes as all p-values are >0.05, suggesting that the distribution of these medical conditions is not significantly different across the three phenotypes.

Figure 15: Distribution of comorbidities across phenotypes

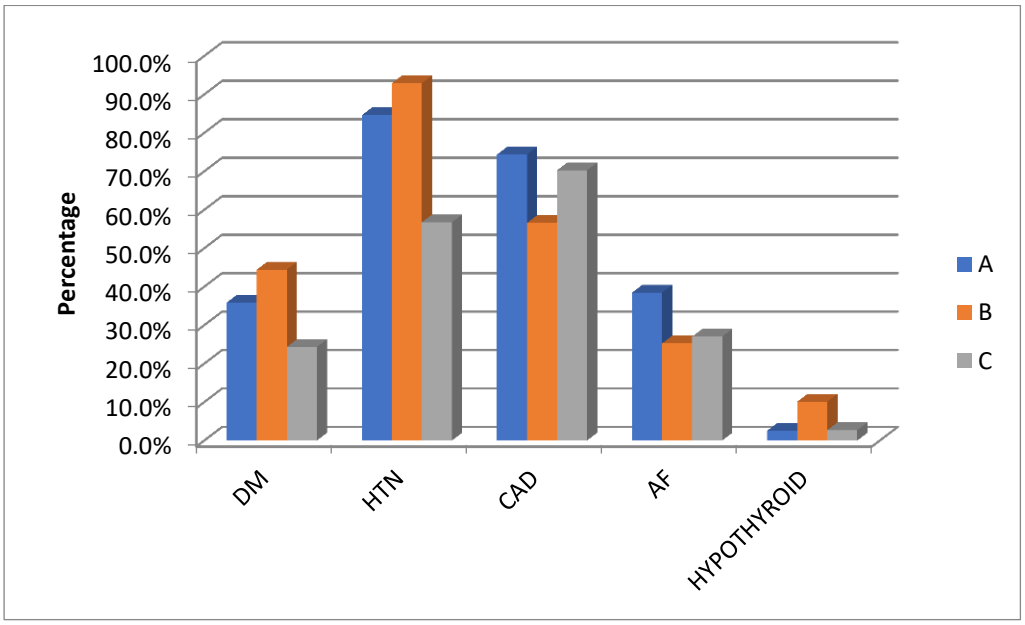


Table 19: Distribution of Cardiovascular Medications across Phenotypes: Analysis of ACEI, ARB, ARNI, SGLT2 Inhibitors, Diuretics, and MRA Usage across phenotypes

	PHENOTYPE	A		B		C		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
ACEI	NO	26	66.7	71	71.7	28	75.7	125	0.764	0.682
	YES	13	33.3	28	28.3	9	24.3	50		
ARB	NO	19	48.7	44	44.4	28	75.7	91	10.742	0.005
	YES	20	51.3	55	55.6	9	24.3	84		
ARNI	NO	38	97.4	99	100.0	22	59.5	159	55.903	0.001
	YES	1	2.6	0	0.0	15	40.5	16		
SGLT2	NO	32	82.1	76	76.8	20	54.1	128	9.101	0.011
	YES	7	17.9	23	23.2	17	45.9	47		

DIURETICS	NO	9	23.1	49	49.5	12	32.4	70	9.256	0.010
	YES	30	76.9	50	50.5	25	67.6	105		
MRA	NO	22	56.4	66	66.7	25	67.6	113	1.471	0.479
	YES	17	43.6	33	33.3	12	32.4	62		
Total		39	100.0	99	100	37	100.0	175		

ACEI (p=0.682) and MRA (p=0.479) show no significant differences across phenotypes. However, significant variations are observed in ARB usage (A: 51.3%, B: 55.6%, C: 24.3%, p=0.005), ARNI usage (A: 2.6%, B: 0%, C: 40.5%, p=0.001), SGLT2 inhibitors (A: 17.9%, B: 23.2%, C: 45.9%, p=0.011), and diuretics (A: 76.9%, B: 50.5%, C: 67.6%, p=0.010). The low p-values (<0.05) for these four medications indicate statistically significant differences in medication patterns across phenotypes.

Figure 16: Distribution of Cardiovascular Medications across Phenotypes: Analysis of ACEI, ARB, ARNI, SGLT2 Inhibitors, Diuretics, and MRA Usage across phenotypes

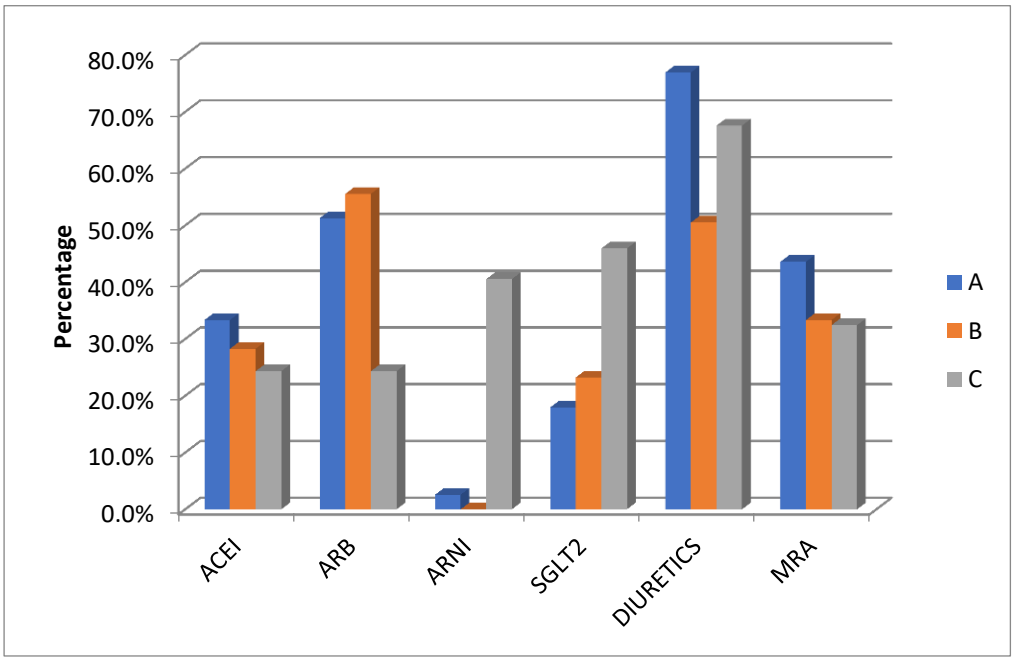


Table 20: Distribution of hospitalization due to heart failure during follow up across phenotypes

	PHENOTYPE	A		B		C		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
No. of hospitalization due to heart failure DURING FOLLOW-UP	NO	22	56.4	75	75.8	29	78.4	126	6.142	0.046
	YES	17	43.6	24	24.2	8	21.6	49		
Total		39	100.0	99	100.0	37	100.0%	175		

Phenotype A shows the highest hospitalization rate (43.6%), while Phenotypes B and C show lower rates (24.2% and 21.6% respectively). The chi-square value of 6.142 with a p-value of 0.046 (<0.05) indicates these differences are statistically significant.

Figure 17: Distribution of hospitalization due to heart failure during follow up across phenotypes

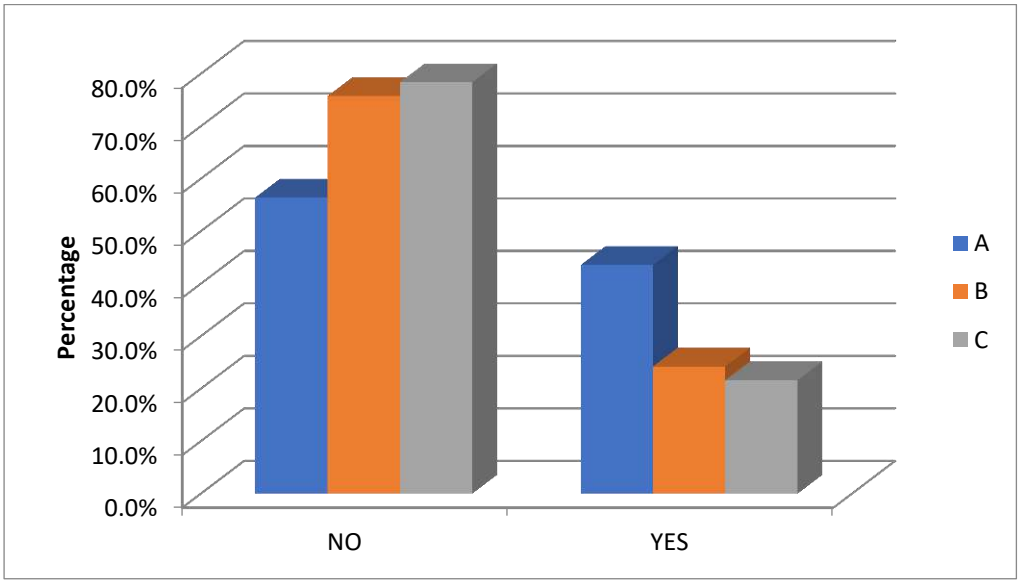


Table 21: Distribution of mortality across phenotypes

	PHENOTYPE	A		B		C		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
Mortality	NO	36	92.3	94	94.9	37	100.0	167	2.695	0.260
	YES	3	7.7	5	5.1	0	0.0	8		
Total		39	100.0	99	100.0	37	100.0	175		

Phenotype A has 7.7% mortality (3 deaths), Phenotype B has 5.1% mortality (5 deaths), and Phenotype C has 0% mortality (no deaths). However, with a chi-square value of 2.695 and p-value of 0.260 (>0.05), these differences are not statistically significant.

Figure 18: Distribution of mortality across phenotypes

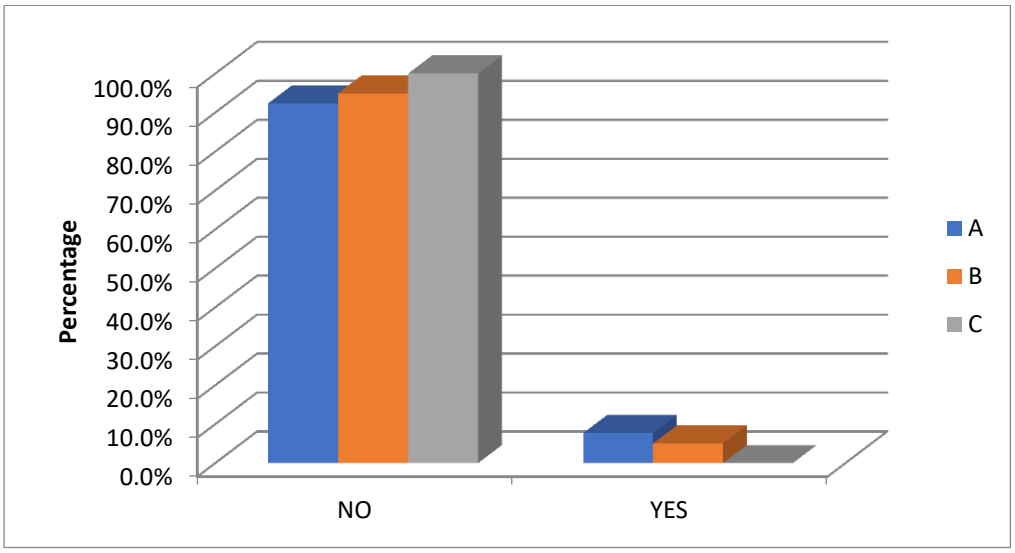


Table 22: Distribution of NYHA CLASS across phenotypes

	PHENOTYPE	A		B		C		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
NYHA CLASS	II	21	53.8	71	71.7	26	70.3	118	4.241	0.12
	III	18	46.2	28	28.3	11	29.7	57		
Total		39	100.0	99	100.0	37	100.0	175		

The distribution shows that Phenotype A has a more even split between Class II (53.8%) and Class III (46.2%), while both Phenotype B (71.7% Class II, 28.3% Class III) and Phenotype C (70.3% Class II, 29.7% Class III) show similar patterns with a predominance of Class II patients. However, with a chi-square value of 4.241 and a p-value of 0.12 (>0.05), these differences are not statistically significant.

Figure 19: Distribution of NYHA CLASS across phenotypes

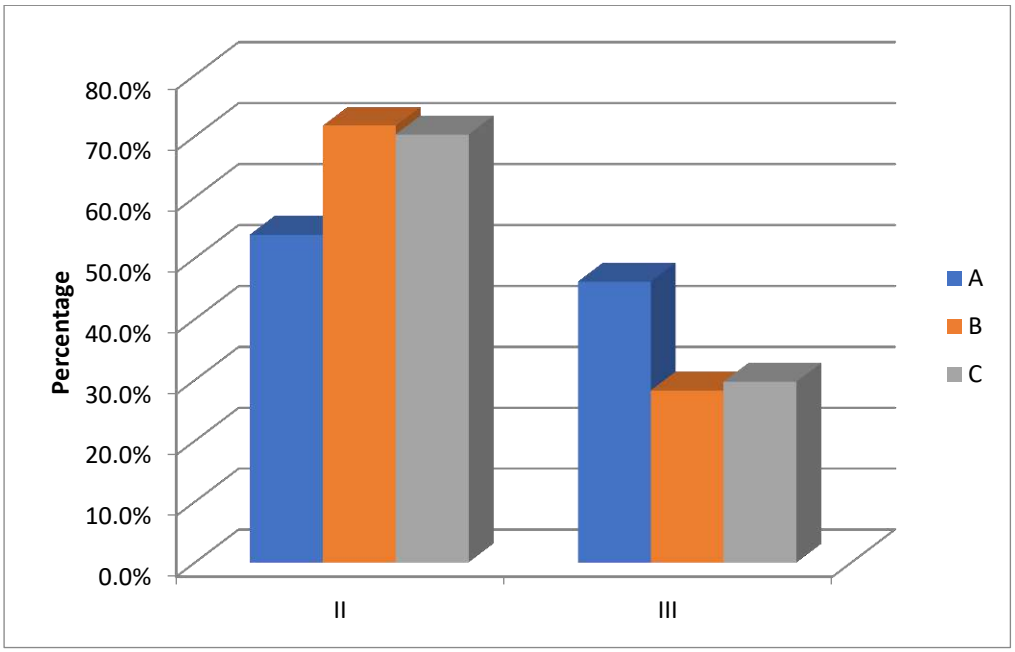


Table 23: NYHA class of patients across different phenotypes (A,B and C) during last follow up visit

	PHENOTYPE	A		B		C		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
NYHA CLASS LAST FOLLOW UP	I	12	30.8%	6	6.1%	15	40.5%	33	30.021	0.001
	II	13	33.3%	55	55.6%	8	21.6%	76		
	III	14	35.9%	36	36.4%	13	35.1%	63		
	IV	0	0.0%	2	2.0%	1	2.7%	3		
Total		39	100.0%	99	100.0%	37	100.0%	175		

Phenotype A shows a relatively even distribution between Class I (30.8%), Class II (33.3%), and Class III (35.9%) with no Class IV cases; Phenotype B shows a predominance in Class II (55.6%) and Class III (36.4%) with Class I (6.1%) and Class IV (2.0%); Phenotype C shows highest proportion in Class I (40.5%), Class II (21.6%) followed by Class III (35.1%), with minimal Class IV (2.7%) The chi-square value of 25.967 with a p-value of 0.001 indicates these differences are statistically significant.

Figure 20: NYHA class of patients across different phenotypes (A, B and C) during last follow up visit

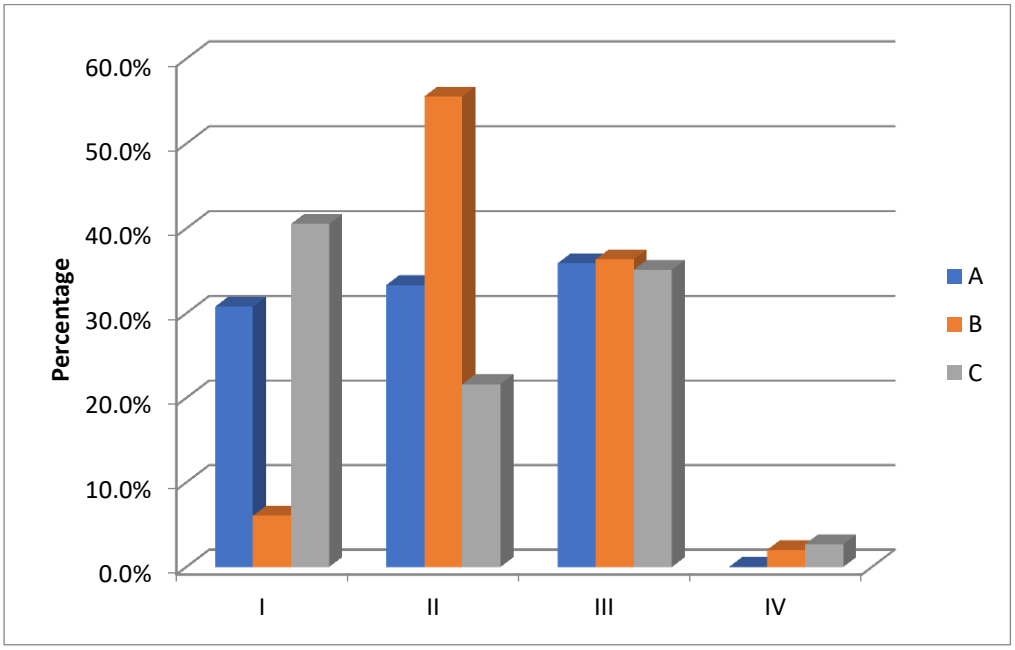


Table 24: Comparison of clinical, laboratory, and functional parameters across three phenotypes (A, B, and C)

	A		B		C		F	p-value	A VS B	A VS C	B VS C
	Mean	SD	Mean	SD	Mean	SD			p-value	p-value	p-value
AGE	74.49	4.63	65.90	4.97	45.24	5.40	353.217	0.001	0.001	0.001	0.001
SBP	135.44	14.34	133.05	15.13	130.32	12.29	1.196	0.305	0.382	0.124	0.327
DBP	80.90	7.95	78.24	10.19	78.78	10.78	1.018	0.363	0.157	0.352	0.776
PR	77.74	12.13	77.12	9.95	75.46	12.86	0.443	0.643	0.767	0.372	0.439
HEIGHT	158.69	9.89	160.76	8.57	159.70	6.42	0.877	0.418	0.199	0.605	0.518
WEIGHT	81.13	14.68	80.78	13.31	80.49	12.48	0.022	0.979	0.892	0.836	0.909
BMI	21.96	2.37	25.17	5.00	24.68	3.50	8.117	0.001	0.001	0.006	0.546
HB	11.52	2.09	12.19	1.30	11.94	1.36	2.816	0.063	0.019	0.231	0.378
Creatinine	1.46	1.19	1.29	0.84	0.95	0.63	3.213	0.043	0.344	0.015	0.048
NTPROBNP	4043.49	685.98	1809.20	304.16	1414.30	190.67	518.624	0.001	0.001	0.001	0.001
EF	60.00	0.00	59.47	2.07	59.86	0.82	1.829	0.164	0.085	0.714	0.209
MITAL E	91.49	27.05	81.96	39.01	92.86	28.59	1.815	0.166	0.149	0.865	0.113
MITRAL A	80.23	33.72	68.77	43.74	79.53	26.28	1.719	0.182	0.121	0.938	0.165
E/A	1.01	0.44	1.04	0.50	1.78	4.01	1.981	0.142	0.934	0.098	0.062

E/E'	17.99	3.34	18.03	6.36	17.83	5.06	0.016	0.984	0.967	0.905	0.858
LA size	43.00	5.59	41.00	6.65	45.00	4.99	5.801	0.004	0.087	0.161	0.001
6 MWT	236.67	103.67	265.64	109.76	290.38	56.72	2.780	0.065	0.126	0.020	0.199
KCCQ	58.41	3.07	49.18	3.41	60.22	3.26	203.719	0.001	0.001	0.018	0.001

Significant differences ($p<0.001$) were found in age distribution, with Phenotype A being the oldest (74.49 years), B intermediate (65.90 years), and C youngest (45.24 years). While vital signs (SBP, DBP, PR) were comparable across groups, BMI showed significant variations with Phenotype A having the lowest (21.96) compared to B and C. Laboratory parameters revealed that Phenotype A had significantly higher NT-proBNP levels (4043.49) and creatinine (1.46) compared to other groups. Echocardiographic parameters showed preserved ejection fraction across all groups (around 60%), but significant differences were noted in LA size and diastolic dysfunction (DD), with Phenotype A showing more severe diastolic dysfunction. Functional capacity assessed by the 6-minute walk test was lowest in Phenotype A (236.67m), and quality of life measured by KCCQ showed significant variations with Phenotype B having the lowest scores (49.18). This suggests three distinct phenotypes with varying age profiles, cardiac biomarkers, diastolic function, and functional capacity despite similar ejection fraction.

Table 25: Comparison of diastolic dysfunction across various phenotypes (A, B and C) during start of enrolment

		A		B		C		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
DD	1	3	7.7%	27	27.3%	13	35.1%	43	9.612	0.047
	2	21	53.8%	46	46.5%	17	45.9%	84		
	3	15	38.5%	26	26.3%	7	18.9%	48		
Total		39	100.0%	99	100.0%	37	100.0%	175		

The above table shows the distribution of diastolic dysfunction across phenotypes. Phenotype A had 7.7% of patients with DD Type I, 53.8% of patients with DD type II, and 38.5% with DD type 3. Phenotype B had 27.3%% of patients with DD Type I, 46.5% of patients with DD type II, and 26.3% with DD type 3. Phenotype C had 35.1 of patients with DD Type I, 45.9 % of patients with DD type II, and 18.9% with DD type 3.

DISCUSSION

This single-center, prospective observational study was conducted in the Hero DMC Heart Institute Department of Cardiology. The sample size included patients with HFpEF during the study period. Patient information was gathered through direct interviews, physical examinations, and medical records. Inclusion criteria encompassed patients ≥18 years old with EF ≥50% and either elevated NT-proBNP levels or a heart failure diagnosis using Framingham criteria. The study used factors such as BMI, hypertension, AF, age, and echocardiographic parameters. Exclusion criteria included severe renal or hepatic impairment, prior EF <50%, specific cardiomyopathies, limited life expectancy, pregnancy, severe anemia, recent cardiac events, uncontrolled blood pressure, and concurrent trial enrollment. The study aimed to EVALUATE different clinical phenotypes of HFpEF patients and correlate these phenotypes with patient outcomes, utilizing statistical methods to analyze relationships between identified clinical results and phenotypes while controlling for confounding variables.

Age and Gender Distribution

We discovered strong correlations between phenotypes and gender and age. Phenotype A was predominantly older (>65 years), Phenotype B had a mixed age distribution, and Phenotype C was exclusively younger (<65 years). These findings align with the study by Shah SJ et al[53], which identified an elderly phenotype with a high prevalence of AF and hypertension, similar to our Phenotype A.

Gender distribution varied significantly across phenotypes, with Phenotype B showing a strong female predominance (85.9%) and Phenotype C a clear male predominance (78.4%). This gender-specific pattern is consistent with findings from Tromp J et al[5], who identified a "female" phenotype characterized by higher rates of hypertension and obesity.

Further supporting our findings, Lam CSP et al[55] conducted a comprehensive review of HFpEF, highlighting that the syndrome is

more common in older adults and women. They noted that up to 50% of heart failure cases in the elderly are HFpEF, which aligns with our Phenotype A's predominance in the older age group. The higher prevalence of HFpEF in women, particularly older women, as observed in our Phenotype B, is consistent with their findings.

A study by Beale AL et al in 2019[56] found a phenotype group characterized by older age, female predominance, and higher rates of hypertension and AF, which closely resembles our Phenotype A. This reinforces the idea that age and gender play crucial roles in defining HFpEF phenotypes.

Interestingly, our Phenotype C, characterized by younger age and male predominance, finds parallels in a study by Segar MW et al[57]. They identified a "young male" phenotype in HFpEF patients, characterized by obesity, diabetes, and coronary artery disease.

The TOPCAT trial, as analyzed by Merrill M et al[58] discovered that HFpEF women were more likely than males to be older, have higher BMI, and have hypertension. This aligns with the characteristics we observed in our Phenotype B. However, they also noted that despite these differences, women had better outcomes than men.

These comparisons underscore the heterogeneity of HFpEF and the importance of considering age and gender in both research and clinical practice.

BMI and Comorbidities

The significant association between BMI and phenotypes in our study, particularly the higher proportions of overweight individuals in Phenotype C, resonates with the findings of Obokata M et al.[59] They described an "obesity phenotype" in HFpEF, characterized by increased plasma volume and more severe cardiac remodeling. Our study found no significant associations between phenotypes and lifestyle factors such as alcohol consumption and smoking. This is in contrast to certain earlier research, such as that by Savji N et al.[60]which suggested a link between these factors and HFpEF risk. The strong association between hypertension and Phenotypes A and B in our study (84.6% and 92.9%, respectively) is consistent with the

findings of Lam CSP et al[55] who emphasized the central role of hypertension in HFpEF pathophysiology.

Medication Patterns

Our research found notable differences in the use of medications across phenotypes, particularly for ARBs, ARNIs, SGLT2 inhibitors, and diuretics. These differences suggest distinct therapeutic approaches for different phenotypes, aligning with the concept of phenotype-specific treatment strategies proposed by Senni M et al[61]

The variation in ARB usage across our phenotypes (A: 51.3%, B: 55.6%, C: 24.3%) is particularly noteworthy. This pattern is consistent with findings from the PARAGON-HF trial, analyzed by Solomon SD et al[62] They found that the efficacy of sacubitril/valsartan varied across subgroups, with greater benefit observed in patients with lower ejection fraction and women. The higher use of ARBs in our Phenotypes A and B, which had higher proportions of women and older patients, aligns with these findings and suggests a potential targeted approach to ARB therapy in HFpEF.

The significant difference in ARNI usage across our phenotypes (A: 2.6%, B: 0%, C: 40.5%) is a striking finding. This design is not the same as what Lund LH et al[63] observed in their analysis of the Swedish Heart Failure Registry. They found that ARNI use in HFpEF was generally low and did not differ substantially across subgroups.

. Our finding of high ARNI use in Phenotype C (younger, male-predominant) suggests a potentially novel approach to treating this subgroup of HFpEF patients that warrants further investigation.

The variation in SGLT2 inhibitor use across our phenotypes (A: 17.9%, B: 23.2%, C: 45.9%) is exciting in light of recent findings. In their analysis of the EMPEROR-Preserved trial, Anker SD et al[64] found that empagliflozin reduced the risk of cardiovascular death or hospitalization for heart failure across the spectrum of HFpEF, regardless of diabetes status. The higher use of SGLT2 inhibitors in our Phenotype C suggests that clinicians may be adopting these medications more rapidly for younger patients, possibly due to the frequent co-occurrence of diabetes in this group.

Our finding of significant differences in diuretic use (A: 76.9%, B: 50.5%, C: 67.6%) aligns with the observations of Kapoor JR et al[65] in their analysis of the TOPCAT trial. They found that diuretic use varied across subgroups of HFpEF patients and was associated with different outcomes. The higher use of diuretics in our Phenotype A, which was predominantly older patients, mirrors their finding that older HFpEF patients were more likely to be on diuretics.

Clinical Outcomes

The significantly higher hospitalization rate in Phenotype A (43.6%) compared to Phenotypes B and C is a crucial finding. This aligns with the results of Pfeffer MA et al,[66] which found that older age and a history of AF (characteristics more common in our Phenotype A) were associated with an increased risk of hospitalization.

Shah et al[53] provide additional support for our findings in their phenomapping study of HFpEF. They identified a phenotype group characterized by older age, renal dysfunction, and high rates of AF, which showed the highest risk of heart failure hospitalization. This group bears similarities to our Phenotype A, reinforcing the idea that certain clinical characteristics may predispose HFpEF patients to higher hospitalization rates.

Remarkably, our findings also reveal similarities with the research conducted by Tromp J et al[5] who conducted a machine-learning analysis of HFpEF patients in the ASIAN-HF registry. They identified six distinct phenotypes, with one group showing characteristics similar to our Phenotype A - older age, high prevalence of AF, and renal dysfunction. This group also demonstrated the highest rate of heart failure hospitalizations, consistent with our findings.

The lower hospitalization rates observed in our Phenotypes B and C (24.2% and 21.6% respectively) are noteworthy. These findings suggest that younger age and potentially better overall health status may be protective against hospitalizations in HFpEF patients. This is consistent with the observations of Lam CSP[55] et al in their analysis of the TOPCAT Americas population, where they found that younger age and female sex (characteristics more prevalent in our Phenotype B)

were associated with lower rates of cardiovascular events, including hospitalizations.

There were no statistically significant variations in mortality rates between phenotypes in our study. (higher mortality in Phenotypes A and B). This trend aligns with findings by Lund LH et al[63]which showed that higher mortality was linked to AF, diabetes, and advanced age in HFpEF patients.

Our finding of significant differences in NYHA class outcomes at follow-up across phenotypes is significant. This suggests that phenotype classification might have prognostic value in predicting functional outcomes, a finding that could have important clinical implications. This aligns with the work of Kao DP et al[67] who found that distinct phenotypes of HFpEF were associated with different trajectories of functional status over time.

Mortality

While our study did not find statistically significant differences in mortality rates across phenotypes, the numerical trend (higher mortality in Phenotypes A and B) warrants further investigation. The study done by Solomon SD et al[37] similarly found that older patients with HFpEF had worse outcomes, although they did not specifically categorize patients into phenotypes.

Our results are consistent with those of Pfeffer MA et al.[66]. They found that among patients with HFpEF, concomitant conditions such as diabetes and prior myocardial infarction, as well as older age and male sex, were linked to increased mortality. This is in line with the pattern we saw in Phenotype A, which was defined by a larger burden of comorbidities and an older age.

Interestingly, Our findings are also consistent with the research conducted by Shah SJ et al[53], who identified different HFpEF phenotypes using machine learning approaches. The highest mortality rates were found in a high-risk phenotype that was defined by advanced age, renal impairment, and a high prevalence of AF. Even though our study did not achieve statistical significance, this phenotype

is similar to our Phenotype A, indicating that some clinical traits may be linked to an increased mortality risk in HFpEF.

The trend towards higher mortality in our Phenotype B, which had a strong female predominance, is intriguing when compared to findings from other studies. Duca F et al[6] conducted a meta-analysis of sex-specific differences in HFpEF outcomes and found that women generally had lower mortality rates than men, despite often being older and having more comorbidities. Our trend, while not statistically significant, suggests that the relationship between gender and mortality in HFpEF may be more complex and potentially influenced by other phenotypic characteristics.

It's worth noting that our Phenotype C, characterized by younger age and male predominance, showed the lowest numerical mortality rate. This aligns with findings from the CHARM-Preserved trial, analyzed by Lund LH et al[63] which demonstrated that younger age was associated with better survival in HFpEF patients. However, they also found that male sex was associated with worse outcomes, highlighting the complex interplay of age and gender in HFpEF prognosis.

The lack of statistical significance in our mortality findings, despite these numerical trends, may be due to several factors. First, our sample size may have been insufficient to detect significant differences, especially given the generally lower event rates in HFpEF compared to HFREF. Second, the follow-up period in our study may not have been long enough to capture meaningful differences in mortality. As noted by Owan TE et al in their long-term study of HFpEF trends, the prognostic impact of different clinical characteristics may become more apparent over extended follow-up periods.

These comparisons underscore the complexity of mortality risk in HFpEF and highlight the need for larger, longer-term studies to fully elucidate the relationship between specific phenotypes and mortality outcomes. Our findings, while not reaching statistical significance, contribute to the ongoing discussion about the heterogeneity of HFpEF and the potential for phenotype-specific risk stratification.

This study contributes to the growing body of evidence supporting the heterogeneity of HFpEF. The identification of distinct phenotypes with unique characteristics and outcomes underscores the need for personalized approaches in both research and clinical management of HFpEF. As we continue to unravel the complexities of this syndrome, phenotype-specific strategies may pave the way for more effective prevention, treatment, and prognostication in HFpEF.

Limitations

Our study has several limitations. As a single-center study, the generalizability of our findings may be limited. The sample size, while adequate for identifying broad patterns, may have been insufficient to detect more subtle associations, particularly in mortality outcomes. Future research should focus on validating these phenotypes in larger, multi-center cohorts. Additionally, longitudinal studies are needed to understand how these phenotypes evolve and respond to different treatment strategies.

SUMMARY AND CONCLUSION

Summary

The present single-center prospective observational study was conducted at Hero DMC Heart Institute's Cardiology Department to study heart failure patients with preserved ejection fraction (HFpEF). The inclusion criteria of Patients were: age ≥18 years, EF ≥50%, elevated NT-proBNP levels (age-dependent thresholds) or heart failure diagnosis using Framingham criteria, and HFpEF confirmation by a cardiologist. Exclusion criteria include end-stage renal disease, severe hepatic impairment, prior EF <50%, specific cardiomyopathies, life expectancy <1 year, pregnancy/lactation, severe anemia, recent cardiac events, uncontrolled BP, and concurrent trial participation; study duration was 1.5 years with statistical analysis using categorical and continuous variables.

- In the present study Phenotype A was strongly associated with older age (97.4% of cases are >65 years), Phenotype B is more evenly distributed between age groups (56.6% >65 years, 43.4% <65 years), while Phenotype C exclusively appears in younger individuals (100% <65 years). The chi-square value of 73.248 and p-value of 0.001 indicate that age group differences are statistically significant.
- Phenotype A shows a relatively balanced distribution between females (56.4%) and males (43.6%), Phenotype B demonstrates a strong female predominance (85.9% female vs 14.1% male), while Phenotype C shows a clear male predominance (78.4% male vs 21.6% female). The chi-square value of 51.256 with a p-value of 0.001 indicates these gender-based differences are statistically significant.
- Phenotype A shows the highest concentration in the normal BMI range (53.8% in 18.5-22.9), with no cases in the obese category (>30); phenotype B shows a notable presence in overweight (45.5%) and obese (18.9%) categories. Phenotype C shows more spread distribution across all BMI ranges with a notable

presence of overweight ranges (35.1% in 23-24.9 and 32.4% in 25-29.9) with no underweight cases. The chi-square value of 24.175 with a p-value of 0.001 indicates these BMI-based differences are statistically significant.

- All phenotypes show low proportions of alcoholics: Phenotype A (2.6%), Phenotype B (10.1%), and Phenotype C (2.7%), with a chi-square value of 3.756 and p-value of 0.153. Similarly, for smoking, all phenotypes show low proportions of smokers: Phenotype A (5.1%), Phenotype B (7.1%), and Phenotype C (5.4%), with a chi-square value of 0.241 and p-value of 0.887. The high p-values (>0.05) for both lifestyle factors indicate that there are no statistically significant associations between phenotypes and alcohol consumption or smoking habits in the study population.
- For DM, the distribution shows varying patterns: Phenotype A (35.9%), Phenotype B (44.4%), and Phenotype C (24.3%) with a chi-square value of 4.736 and p-value of 0.094, indicating no statistically significant association. However, for HTN, there's a significant variation: Phenotype A (84.6%), Phenotype B (92.9%), and Phenotype C (56.8%) with a chi-square value of 25.542 and p-value of 0.001, indicating a strong statistical association between phenotypes and hypertension, with Phenotypes A and B showing notably higher proportions of hypertensive cases compared to Phenotype C.
- For revascularization, all phenotypes show relatively low rates (A: 10.3%, B: 10.1%, C: 21.6%, p=0.174); Coronary Artery Disease (CAD) shows high prevalence across all phenotypes (A: 74.4%, B: 56.6%, C: 70.3%, p=0.067); AF varies among phenotypes (A: 38.5%, B: 25.3%, C: 27.0%, p=0.294); and hypothyroidism shows low prevalence (A: 2.6%, B: 10.1%, C: 2.7%, p=0.153). Notably, none of these conditions show statistically significant associations with phenotypes as all p-values are >0.05, suggesting that the distribution of these

medical conditions is not significantly different across the three phenotypes.

- ACEI (p=0.682) and MRA (p=0.479) show no significant differences across phenotypes. However, significant variations are observed in: ARB usage (A: 51.3%, B: 55.6%, C: 24.3%, p=0.005), ARNI usage (A: 2.6%, B: 0%, C: 40.5%, p=0.001), SGLT2 inhibitors (A: 17.9%, B: 23.2%, C: 45.9%, p=0.011), and diuretics (A: 76.9%, B: 50.5%, C: 67.6%, p=0.010). The low p-values (<0.05) for these four medications indicate statistically significant differences in medication patterns across phenotypes.
- Phenotype A shows the highest hospitalization rate (43.6%), while Phenotypes B and C show lower rates (24.2% and 21.6% respectively). The chi-square value of 6.142 with a p-value of 0.046 (<0.05) indicates these differences are statistically significant.
- Phenotype A has 7.7% mortality (3 deaths), Phenotype B has 5.1% mortality (5 deaths), while Phenotype C has 0% mortality (no deaths). However, with a chi-square value of 2.695 and p-value of 0.260 (>0.05), these differences are not statistically significant.
- The distribution shows that Phenotype A has a more even split between Class II (53.8%) and Class III (46.2%), while both Phenotype B (71.7% Class II, 28.3% Class III) and Phenotype C (70.3% Class II, 29.7% Class III) show similar patterns with a predominance of Class II patients. However, with a chi-square value of 4.241 and a p-value of 0.12 (>0.05), these differences are not statistically significant.
- Phenotype A shows a relatively even distribution between Class I (30.8%), Class II (33.3%), and Class III (35.9%) with no Class IV cases; Phenotype B shows a predominance in Class II (55.6%) and Class III (36.4%) with Class I (6.1%) and Class IV (2.0%); Phenotype C shows highest proportion in Class I

(40.5%), Class II (21.6%) followed by Class III (35.1%), with minimal Class IV (2.7%) The chi-square value of 25.967 with a p-value of 0.001 indicates these differences are statistically significant.

Conclusion

The present study provides valuable insights into the heterogeneous nature of HFpEF (HFpEF), revealing distinct phenotypes with unique characteristics, treatment patterns, and outcomes. Three clear phenotypes emerged from the analysis, each with distinctive demographic and clinical profiles: an older group (Phenotype A), a female-predominant group (Phenotype B), and a younger male-predominant group (Phenotype C).

The findings demonstrate significant variations in medication usage and clinical outcomes across these phenotypes, particularly in hospitalization rates. The higher hospitalization rate in Phenotype A (43.6%) compared to Phenotypes B and C suggests that older age and associated comorbidities may contribute to poorer outcomes. While mortality differences weren't statistically significant, the observed trends warrant further investigation in larger cohorts.

The study's findings align with and build upon previous research, contributing to the growing understanding that HFpEF is not a uniform condition but rather a syndrome with multiple distinct presentations. This heterogeneity has important implications for clinical practice, suggesting that a one-size-fits-all approach may be suboptimal. Instead, treatment strategies might benefit from being tailored to specific phenotypes.

To sum up, this study is a significant step in the direction of more individualized HFpEF care strategies. While further study is required to fully realize this promise, the identification of unique phenotypes may open the door to more focused therapy approaches and better patient outcomes.

BIBLIOGRAPHY

1. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021;42:3599-3726.
2. Borlaug BA. Evaluation and management of HFpEF. Nature Reviews Cardiology. 2020;17:559-73.
3. Luchi RJ, Snow E, Luchi JM, Nelson CL, Pircher FJ. Left ventricular function in hospitalized geriatric patients. J Am Geriatr Soc. 1982;30:700-5.
4. Pop C, Ștefan MG, Muntean DM, Stoicescu L, Gal AF, Kiss B, et al. Protective effects of a discontinuous treatment with alpha-lipoic acid in obesity-related HFpEF, in rats. Antioxidants. 2020;9:1073.
5. Teramoto K, Teng TH, Chandramouli C, Tromp J, Sakata Y, Lam CS. Epidemiology and clinical features of HFpEF. Cardiac failure review. 2022;8:e27.
6. Sanjay G, Jeemon P, Agarwal A, Viswanathan S, Sreedharan M, Vijayaraghavan G, et al. In-hospital and three-year outcomes of heart failure patients in South India: the Trivandrum Heart Failure Registry. Journal of cardiac failure. 2018;24:842-8.
7. Teramoto K, Ouwerkerk W, Tay WT, Tromp J, Katherine Teng TH, Chandramouli C, et al. Clinical features of heart failure with normal ejection fraction: insights from the ASIAN-HF registry. JACC: Asia. 2023;3:739-51.
8. Duca F, Zotter-Tufaro C, Kammerlander AA, Aschauer S, Binder C, Mascherbauer J, et al. Gender-related differences in HFpEF. Scientific reports. 2018;8:1080.
9. Kristensen SL, Mogensen UM, Jhund PS, Petrie MC, Preiss D, Win S, et al. Clinical and echocardiographic characteristics and cardiovascular outcomes according to diabetes status in patients with heart failure and preserved ejection fraction: a report from the I-Preserve Trial (Irbesartan in HFpEF). Circulation. 2017;135:724-35.

10. Van Woerden G, van Veldhuisen DJ, Gorter TM, van Empel VP, Hemels ME, Hazebroek EJ, et al. Importance of epicardial adipose tissue localization using cardiac magnetic resonance imaging in patients with heart failure with mid-range and preserved ejection fraction. Clinical Cardiology. 2021;44:987-93.
11. Rech M, Barandiarán Aizpurua A, van Empel V, van Bilsen M, Schroen B. Pathophysiological understanding of HFpEF: microRNAs as part of the puzzle. Cardiovascular Research. 2018;114:782-93.
12. Hicks KA, Mahaffey KW, Mehran R, Nissen SE, Wiviott SD, Dunn B, et al. 2017 Cardiovascular and stroke endpoint definitions for clinical trials. Circulation. 2018;137:961-72.
13. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Drazner MH, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Journal of the American college of cardiology. 2013;62:e147-239.
14. Radulescu D, Stoicescu L, Buzdugan E, Donca V. Patterns of left ventricular remodeling among patients with essential and secondary hypertension. Rev. méd. Chile. 2013:141;1520-7.
15. Dai DF, Chen T, Johnson SC, Szeto H, Rabinovitch PS. Cardiac aging: from molecular mechanisms to significance in human health and disease. Antioxidants & redox signaling. 2012;16:1492-526.
16. Liu S, Guan Z, Jin X, Meng P, Wang Y, Zheng X, et al. Left ventricular diastolic and systolic dyssynchrony and dysfunction in HFpEF and a narrow QRS complex. International journal of medical sciences. 2018;15:108-14.
17. Santos AB, Kraigher-Krainer E, Bello N, Claggett B, Zile MR, Pieske B, et al. Left ventricular dyssynchrony in patients with heart failure and preserved ejection fraction. European Heart Journal. 2014;35:42-7.

18. Melenovsky V, Hwang SJ, Lin G, Redfield MM, Borlaug BA. Right heart dysfunction in HFpEF. European Heart Journal. 2014;35:3452-62.
19. Paulus WJ, Tschöpe C. A novel paradigm for HFpEF: comorbidities drive myocardial dysfunction and remodeling through coronary microvascular endothelial inflammation. Journal of the American College of Cardiology. 2013;62:263-71.
20. Cao N, Wong YG, Rosli S, Kiriazis H, Huynh K, Qin C, et al. Chronic administration of the nitroxyl donor 1-nitrosocyclo hexyl acetate limits left ventricular diastolic dysfunction in a mouse model of diabetes mellitus in vivo. Circulation: Heart Failure. 2015;8:572-81.
21. Sarma S, Stoller D, Hendrix J, Howden E, Lawley J, Livingston S, et al. Mechanisms of chronotropic incompetence in HFpEF. Circulation: Heart Failure. 2020;13:e006331.
22. Li C, Qin D, Hu J, Yang Y, Hu D, Yu B. Inflamed adipose tissue: A culprit underlying obesity and HFpEF. Frontiers in immunology. 2022;13:947147.
23. Xiao W, Oldham WM, Priolo C, Pandey AK, Loscalzo J. Immunometabolic endothelial phenotypes: integrating inflammation and glucose metabolism. Circulation research. 2021;129:9-29.
24. Van Aelst LN, Arrigo M, Placido R, Akiyama E, Girerd N, Zannad F, et al. Acutely decompensated heart failure with preserved and reduced ejection fraction present with comparable hemodynamic congestion. European journal of heart failure. 2018;20:738-47.
25. Fallick C, Sobotka PA, Dunlap ME. Sympathetically mediated changes in capacitance: redistribution of the venous reservoir as a cause of decompensation. Circulation: Heart Failure. 2011;4:669-75.
26. Banerjee P, Clark AL, Cleland JG. Diastolic heart failure: a difficult problem in the elderly. The American journal of geriatric cardiology. 2004;13:16-21.
27. Kawaguchi M, Hay I, Fetics B, Kass DA. Combined ventricular systolic and arterial stiffening in patients with heart failure and

preserved ejection fraction: implications for systolic and diastolic reserve limitations. Circulation. 2003;107:714-20.

28. Neeland IJ, Gupta S, Ayers CR, Turer AT, Rame JE, Das SR, et al. Relation of regional fat distribution to left ventricular structure and function. Circulation: Cardiovascular Imaging. 2013;6:800-7.
29. Weisbrod RM, Shiang T, Al Sayah L, Fry JL, Bajpai S, Reinhart-King CA, et al. Arterial stiffening precedes systolic hypertension in diet-induced obesity. Hypertension. 2013;62:1105-10.
30. Alpert MA, Lambert CR, Panayiotou H, Terry BE, Cohen MV, Massey CV, et al. Relation of the duration of morbid obesity to left ventricular mass, systolic function, and diastolic filling, and effect of weight loss. The American journal of cardiology. 1995;76:1194-7.
31. Gupta DK, Shah AM, Castagno D, Takeuchi M, Loehr LR, Fox ER, et al. HFpEF in African Americans: the ARIC (Atherosclerosis Risk In Communities) study. JACC: Heart Failure. 2013;1:156-63.
32. Mentz RJ, Broderick S, Shaw LK, Fiuzat M, O'Connor CM. HFpEF: comparison of patients with and without angina pectoris (from the Duke Databank for Cardiovascular Disease). Journal of the American College of Cardiology. 2014;63:251-8.
33. Lee PW, Zhang Q, Yip GW, Wu L, Lam YY, Wu EB, et al. Left ventricular systolic and diastolic dyssynchrony in coronary artery disease with preserved ejection fraction. Clinical science. 2009;116:521-9.
34. Kim MM, Prasad M, Burton Y, Kolseth CM, Zhao Y, Chandrashekar P, et al. Comparative Outcomes of a Transthyretin Amyloid Cardiomyopathy Cohort Versus Patients With Heart Failure With Preserved Ejection Fraction Enrolled in the TOPCAT Trial. J Am Heart Assoc. 2023;12:e029705.
35. Baker WL, Smyth LR, Riche DM, Bourret EM, Chamberlin KW, White WB. Effects of sodium-glucose co-transporter 2 inhibitors on blood pressure: a systematic review and meta-analysis. Journal of the American Society of Hypertension. 2014;8:262-75.

36. Ferrannini E, Mark M, Mayoux E. CV protection in the EMPA-REG OUTCOME trial: a “thrifty substrate” hypothesis. Diabetes care. 2016;39:1108-14.
37. Solomon SD, McMurray JJ, Claggett B, de Boer RA, DeMets D, Hernandez AF, et al. Dapagliflozin in heart failure with mildly reduced or preserved ejection fraction. New England Journal of Medicine. 2022;387:1089-98.
38. Tamargo J. Sodium-glucose cotransporter 2 inhibitors in heart failure: potential mechanisms of action, adverse effects, and future developments. European Cardiology Review. 2019;14:23.
39. Hasenfuß G, Hayward C, Burkhoff D, Silvestry FE, McKenzie S, Gustafsson F, Malek F, Van der Heyden J, Lang I, Petrie MC, Cleland JG. A transcatheter intracardiac shunt device for HFpEF (REDUCE LAP-HF): a multicentre, open-label, single-arm, phase 1 trial. The Lancet. 2016;387:1298-304.
40. Pierre-Jean M, Marut B, Curtis E, Galli E, Cuggia M, Bouzillé G, et al. Phenotyping of heart failure with preserved ejection fraction using electronic health records and echocardiography. European Heart Journal Open. 2024;4:oead133.
41. Xu X, Wang Y, Li Y, Zhang B. Clinical phenotypic characteristics of HFpEF and its influence on prognosis.
42. Anker SD, Usman MS, Anker MS, Butler J, Böhm M, Abraham WT, et al. Patient phenotype profiling in HFpEF to guide therapeutic decision making. A scientific statement of the Heart Failure Association, the European Heart Rhythm Association of the European Society of Cardiology, and the European Society of Hypertension. European journal of heart failure. 2023;25:936-55.
43. Nguyen NT, Tran DT, Le An P, Van Hoang S, Nguyen HA, Chau HN. Clinical Phenotypes and Age-Related Differences in Presentation, Treatment, and Outcome of HFpEF: A Vietnamese Multicenter Research. Cardiology Research and Practice. 2021;2021:4587678.
44. Mitic VT, Stojanovic DR, Ilic MZ, Stojanovic MM, Petrovic DB, Ignjatovic AM, et al. Cardiac remodeling biomarkers as potential

circulating markers of left ventricular hypertrophy in HFpEF. The Tohoku Journal of Experimental Medicine. 2020;250:233-42.

45. Fragasso G. The Concept of" HFpEF": Time for a Critical Reappraisal. Reviews in Cardiovascular Medicine. 2023;24:202.
46. Shariff RE, Koh HB, Sulong MA, Quah WJ, Ong SH, Sabian IS, et al. Acute decompensated HFpEF: do the Asian phenotypes fit. J Asian Pacific Soc Cardiol. 2023;2:e07.
47. Tah S, Valderrama M, Afzal M, Iqbal J, Farooq A, Lak MA, et al. HFpEF: An Evolving Understanding. Cureus. 2023;15: e46152.
48. Heinzel FR, Shah SJ. The future of HFpEF: Deep phenotyping for targeted therapeutics. Herz. 2022;47:308-23.
49. Reddy YN, Kaye DM, Handoko ML, Van De Bovenkamp AA, Tedford RJ, Keck C, Andersen MJ, Sharma K, Trivedi RK, Carter RE, Obokata M. Diagnosis of HFpEF among patients with unexplained dyspnea. JAMA cardiology. 2022;7:891-9.
50. Gulea C, Zakeri R, Quint JK. Differences in outcomes between heart failure phenotypes in patients with coexistent chronic obstructive pulmonary disease: a cohort study. Annals of the American Thoracic Society. 2022;19:971-80.
51. Cohen JB, Schrauben SJ, Zhao L, Basso MD, Cvijic ME, Li Z, et al. Clinical phenogroups in HFpEF: detailed phenotypes, prognosis, and response to spironolactone. Heart failure. 2020;8:172-84.
52. Hedman ÅK, Hage C, Sharma A, Brosnan MJ, Buckbinder L, Gan LM, et al. Identification of novel pheno-groups in HFpEF using machine learning. Heart. 2020;106:342-9.
53. Shah SJ, Katz DH, Selvaraj S, Burke MA, Yancy CW, Gheorghiade M, et al. Phenomapping for novel classification of HFpEF. Circulation. 2015;131:269-79.
54. Bhatia RS, Tu JV, Lee DS, Austin PC, Fang J, Haouzi A, et al. Outcome of HFpEF in a population-based study. New England Journal of Medicine. 2006;355:260-9.

55. Lam CS, Voors AA, de Boer RA, Solomon SD, van Veldhuisen DJ. Heart failure with preserved ejection fraction: from mechanisms to therapies. European heart journal. 2018;39:2780-92.
56. Beale AL, Nanayakkara S, Segan L, Mariani JA, Maeder MT, van Empel V, et al. Sex differences in heart failure with preserved ejection fraction pathophysiology: a detailed invasive hemodynamic and echocardiographic analysis. JACC: Heart Failure. 2019;7:239-49.
57. Segar MW, Patel KV, Berry JD, Grodin JL, Pandey A. Generalizability and implications of the H2FPEF score in a cohort of patients with heart failure with preserved ejection fraction: insights from the TOPCAT trial. Circulation. 2019;139:1851-3.
58. Merrill M, Sweitzer NK, Lindenfeld J, Kao DP. Sex differences in outcomes and responses to spironolactone in heart failure with preserved ejection fraction: a secondary analysis of TOPCAT trial. JACC: Heart Failure. 2019;7:228-38.
59. Obokata M, Kane GC, Reddy YN, Olson TP, Melenovsky V, Borlaug BA. Role of diastolic stress testing in the evaluation for heart failure with preserved ejection fraction: a simultaneous invasive-echocardiographic study. Circulation. 2017;135:825-38.
60. Savji N, Meijers WC, Bartz TM, Bhambhani V, Cushman M, Nayor M, et al. The association of obesity and cardiometabolic traits with incident HFpEF and HFrEF. JACC: Heart Failure. 2018;6:701-9.
61. Senni M, Paulus WJ, Gavazzi A, Fraser AG, Díez J, Solomon SD, et al. New strategies for heart failure with preserved ejection fraction: the importance of targeted therapies for heart failure phenotypes. European heart journal. 2014;35:2797-815.
62. Solomon SD, Rizkala AR, Gong J, Wang W, Anand IS, Ge J, et al. Angiotensin receptor neprilysin inhibition in heart failure with preserved ejection fraction: rationale and design of the PARAGON-HF trial. JACC: Heart Failure. 2017;5:471-82.
63. Lund LH, Benson L, Dahlström U, Edner M. Association between use of renin-angiotensin system antagonists and mortality in

patients with heart failure and preserved ejection fraction. Jama. 2012;308:2108-17.

64. Anker SD, Butler J, Usman MS, Filippatos G, Ferreira JP, Bocchi E, et al. Efficacy of empagliflozin in heart failure with preserved versus mid-range ejection fraction: a pre-specified analysis of EMPEROR-Preserved. Nature medicine. 2022;28:2512-20.
65. Shah AM, Shah SJ, Anand IS, Sweitzer NK, O'Meara E, Heitner JF, et al. Cardiac structure and function in heart failure with preserved ejection fraction: baseline findings from the echocardiographic study of the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist trial. Circulation: Heart Failure. 2014;7:104-15.
66. Pfeffer MA, Shah AM, Borlaug BA. Heart failure with preserved ejection fraction in perspective. Circulation research. 2019;124:1598-617.
67. Kao DP, Lewsey JD, Anand IS, Massie BM, Zile MR, Carson PE, et al. Characterization of subgroups of heart failure patients with preserved ejection fraction with possible implications for prognosis and treatment response. European journal of heart failure. 2015;17:925-35.

SR NO	Initials	MRD	PHENOTYPE	AGE	AGE GROUP	SEX	SBP	DBP	PR	BMI	BMI GROUP	ALCOHOLIC	SMOKER	DM	HTN	CAD	REVASCULARISATION
1	GK	897475	A	70	2	M	140	90	75	22	2	NO	NO	NO	YES	YES	YES
2	HK	731709	A	60	1	M	140	80	80	20	2	NO	NO	NO	YES	YES	NO
3	SC	406404	A	72	2	F	130	90	91	24	3	NO	NO	NO	YES	YES	NO
4	MK	1635485	A	65	2	F	130	90	80	25	4	NO	NO	NO	YES	YES	NO
5	GS	1611891	A	76	2	M	130	70	76	20	2	NO	NO	NO	YES	YES	YES
6	AR	1646844	A	75	2	M	130	87	69	21	2	NO	NO	YES	YES	YES	NO
7	SS	4812	A	73	2	F	110	60	84	23	3	NO	NO	NO	YES	YES	NO
8	SD	237692	A	77	2	M	140	78	82	23	3	NO	NO	NO	YES	YES	NO
9	RSD	1631072	A	74	2	M	140	80	51	17	1	NO	NO	YES	YES	YES	NO
10	RK	1645303	A	77	2	F	110	70	60	20	2	NO	NO	NO	NO	NO	NO
11	SP	1389156	A	72	2	F	144	64	73	21	2	NO	NO	YES	YES	YES	YES
12	PD	1651582	A	78	2	M	130	90	79	18	1	NO	NO	YES	YES	NO	NO
13	HS	1365570	A	81	2	M	146	88	66	22	2	NO	YES	YES	YES	NO	NO
14	ND	1651021	A	74	2	F	146	86	77	24	3	NO	NO	NO	NO	NO	NO
15	BS	1648138	A	68	2	M	168	78	75	21	2	NO	NO	YES	YES	YES	NO
16	DK	1663070	A	76	2	M	152	84	108	20	2	NO	NO	YES	YES	YES	YES
17	VD	1661687	A	80	2	F	142	82	76	18	1	NO	NO	YES	YES	YES	NO
18	SR	1658348	A	78	2	F	166	92	71	26	4	NO	NO	NO	YES	YES	NO
19	JK	3706	A	77	2	M	140	84	84	24	3	NO	NO	NO	NO	YES	NO
20	AK	1656064	A	73	2	F	126	80	72	27	4	NO	NO	YES	YES	YES	NO
21	SS	1673468	A	71	2	F	110	70	79	25	4	NO	NO	NO	YES	YES	NO
22	JLO	984847	A	80	2	M	138	78	87	21	2	YES	NO	YES	YES	YES	NO
23	SK	314517	A	78	2	F	142	84	51	21	2	NO	NO	NO	YES	YES	NO
24	PM	929889	A	71	2	F	140	70	81	20	2	NO	NO	NO	YES	YES	NO
25	DK	1520440	A	70	2	M	112	70	76	25	4	NO	NO	NO	YES	NO	NO
26	LA	1681977	A	77	2	F	136	82	76	24	3	NO	NO	NO	YES	NO	NO
27	JK	1681578	A	75	2	M	120	80	70	23	3	NO	NO	NO	YES	NO	NO
28	Ap	1669364	A	80	2	F	110	70	78	26	4	NO	NO	YES	NO	NO	NO
29	JK	911508	A	74	2	M	130	80	108	24	3	NO	NO	NO	YES	NO	NO
30	NR	167480	A	73	2	F	156	80	74	20	2	NO	NO	YES	YES	YES	NO
31	SK	1554714	A	75	2	F	140	90	98	20	2	NO	NO	NO	YES	NO	NO
32	DS	196914	A	76	2	M	156	88	68	21	2	NO	NO	YES	YES	YES	NO
33	HP	1677988	A	75	2	F	124	80	82	20	2	NO	NO	NO	YES	YES	NO
34	KG	699280	A	74	2	F	146	80	68	21	2	NO	NO	NO	YES	YES	NO
35	SR	1680744	A	66	2	F	122	84	97	24.3	3	NO	NO	NO	NO	YES	NO
36	MK	262519	A	75	2	F	140	86	76	21.2	2	NO	NO	NO	YES	YES	NO
37	DR	224415	A	79	2	M	130	90	70	22	2	NO	YES	YES	YES	YES	NO
38	TS	1694338	A	76	2	F	140	80	74	22	2	NO	NO	NO	YES	YES	NO
39	N	1660914	A	84	2	F	130	90	90	20	2	NO	NO	NO	NO	YES	NO
40	HK	1663879	B	72	2	M	140	70	69	32	5	NO	NO	NO	NO	YES	YES
41	S	1721813	B	60	1	F	130	80	74	33	5	NO	NO	YES	YES	NO	NO
42	DJ	1719764	B	70	2	F	140	80	70	35	5	NO	NO	YES	YES	NO	NO
43	RK	1396643	B	73	2	F	130	74	69	37	5	NO	NO	YES	YES	YES	NO
44	BKG	1713015	B	70	2	M	110	70	96	34	5	NO	NO	YES	YES	YES	NO

SR NO	Initials	MRD	AF	HYPOTHYROID	HB	creatinine	NTPROBNP	EF	MITAL E	MITRAL A	E/A	E/E'	LA size	TR	DD	6 MWT
1	GK	897475	NO	NO	12.6	3.2	3800	60	102	96	1	14	42	2.8	2	86
2	HK	731709	NO	NO	11	0.1	3540	60	104	112	0.9	18	42	2.8	2	120
3	SC	406404	NO	NO	12.9	0.6	4166	60	70	79	0.8	17	41	2.8	3	250
4	MK	1635485	NO	NO	12.9	0.1	4150	60	74	66	1.1	20	45	30	3	86
5	GS	1611891	NO	NO	17.3	0.2	4360	60	69	66	1	15.2	46	30	3	286
6	AR	1646844	NO	NO	10.6	0.67	4230	60	76	97	0.8	16	29	30	2	94
7	SS	4812	NO	NO	10.5	2.9	4680	60	93	93	1	14	44	30	3	80
8	SD	237692	YES	NO	9.8	0.6	3730	60	92	78	1.2	15	44	50	2	160
9	RSD	1631072	NO	NO	14.9	1.8	4130	60	51	78	0.6	23	44	24	3	246
10	RK	1645303	NO	NO	7.2	0.1	6470	60	87	84	1	26	54	40	3	60
11	SP	1389156	YES	NO	12.9	2.6	4090	60	78	125	0.6	15	43	28	2	480
12	PD	1651582	NO	NO	9	1.8	5050	60	129	132	0.9	16	43	32	2	300
13	HS	1365570	YES	NO	12	0.6	4247	60	97	0		17	41	30	2	126
14	ND	1651021	YES	NO	7.4	2.3	4570	60	140	104	1.3	20	47	30	3	90.00
15	BS	1648138	NO	NO	12.4	0.4	4040	60	77	95	0.8	16	43	30	2	320
16	DK	1663070	YES	NO	8.4	2.6	5050	60	69	92	0.7	16	33	30	2	360
17	VD	1661687	NO	NO	12.1	0.1	3604	60	70	83	0.8	17	46	30	1	200
18	SR	1658348	YES	NO	9.4	0.6	4290	60	120	72	1.6	18	46	50	3	268
19	JK	3706	NO	NO	14	0.8	4213	60	57	114	0.5	20	41	24	2	380
20	AK	1656064	YES	NO	9.9	1.9	4064	60	130	0		28	48	40	1	220
21	SS	1673468	NO	NO	13.3	4.7	4179	60	57	108	0.5	18.7	34	28	2	140
22	JLO	984847	YES	NO	12.1	2.8	2467.2	60	141	0		17	48	32	2	328
23	SK	314517	NO	NO	13.2	3.1	4131	60	72	115	0.6	20	43	30	3	240
24	PM	929889	NO	NO	12	1.9	4154	60	74	65	1.1	20	34	44	2	240
25	DK	1520440	YES	YES	10.2	0.7	3205	60	115	91	1.2	26	41	38	3	175
26	LA	1681977	NO	NO	12.4	0.7	4212	60	83	86	0.9	15.6	55	36	3	280
27	JK	1681578	YES	NO	13	3.5	4149	60	56	91	0.6	18.9	47	32	3	80
28	Ap	1669364	NO	NO	11.9	2.6	4148	60	71	82	0.8	15.5	40	42	3	400
29	JK	911508	YES	NO	10.3	3.2	4134	60	103	83	1.2	15.5	34	48	2	270
30	NR	167480	NO	NO	8.5	2.3	3714	60	132	129	1	17.6	48	22	2	240
31	SK	1554714	NO	NO	10.2	0.5	4386	60	116	98	1.2	18	45	32	2	320
32	DS	196914	YES	NO	11	1.8	3790	60	147	50	3	21.7	44	42	2	280
33	HP	1677988	NO	NO	11.8	0.78	4129	60	77	77	1	14.6	42	48	2	280
34	KG	699280	YES	NO	12.1	0.6	3640	60	112	71	1.6	18	47	22	3	280
35	SR	1680744	NO	NO	11.4	0.9	3990	60	82	116	0.7	14.7	42	44	2	215
36	MK	262519	YES	NO	12.6	0.5	3147	60	59	49	1.2	16.7	31	38	3	270
37	DR	224415	NO	NO	14.4	0.7	3940	60	80	72	1.1	20	49	36	2	280
38	TS	1694338	YES	NO	8.7	0.9	2152	60	130	0		16.8	46	32	1	300.00
39	N	1660914	NO	NO	12.8	0.6	3555	60	76	80	0.94	15	45	42	2	400
40	HK	1663879	NO	NO	11.2	0.9	1850	60	96	136	0.7	24.2	52	45	3	206
41	S	1721813	NO	NO	13.2	0.9	1970	60	83	86	0.9	15.7	58	36	2	286
42	DJ	1719764	NO	NO	12.8	1	1341	60	70	83	0.8	18	52	28	2	320
43	RK	1396643	NO	NO	11.9	1	1535	60	97	70	1.3	14	39	32	2	280
44	BKG	1713015	YES	NO	11.1	1	1740	60	162	0		14.3	48	30	2	206

SR NO	Initials	MRD	KCCQ	ACEI	ARB	ARNI	SGLT2	DIURETICS	MRA	No. of hospitalization due to heart failure DURING FOLLOW UP	Mortality	NYHA CLASS	NYHA CLASS LAST FOLLOW UP
1	GK	897475	60	YES	NO	NO	NO	NO	YES	YES	NO	III	III
2	HK	731709	58	YES	NO	NO	NO	YES	NO	NO	NO	II	III
3	SC	406404	62	YES	NO	NO	YES	YES	NO	YES	NO	III	II
4	MK	1635485	58	NO	YES	NO	NO	YES	NO	YES	NO	III	III
5	GS	1611891	59	YES	NO	NO	NO	YES	NO	NO	NO	II	II
6	AR	1646844	58	NO	YES	NO	NO	YES	NO	NO	NO	II	II
7	SS	4812	61	YES	NO	NO	NO	YES	YES	NO	NO	III	III
8	SD	237692	57	NO	YES	NO	NO	YES	NO	YES	YES	II	III
9	RSD	1631072	60	YES	NO	NO	NO	YES	NO	NO	NO	II	II
10	RK	1645303	58	NO	NO	NO	NO	YES	NO	YES	NO	III	III
11	SP	1389156	64	YES	NO	NO	YES	NO	YES	NO	NO	II	II
12	PD	1651582	62	YES	NO	NO	NO	YES	NO	NO	NO	II	II
13	HS	1365570	58	NO	YES	NO	NO	YES	YES	NO	NO	II	II
14	ND	1651021	60	NO	NO	NO	NO	YES	NO	YES	YES	III	III
15	BS	1648138	59	YES	NO	NO	YES	YES	NO	NO	NO	II	II
16	DK	1663070	60	NO	YES	NO	NO	YES	NO	NO	NO	II	I
17	VD	1661687	56	NO	YES	NO	YES	YES	YES	NO	NO	II	I
18	SR	1658348	58	YES	NO	NO	NO	YES	NO	YES	NO	III	I
19	JK	3706	55	NO	NO	NO	YES	YES	NO	NO	NO	II	I
20	AK	1656064	59	NO	YES	NO	YES	YES	NO	YES	NO	III	II
21	SS	1673468	57	NO	YES	NO	NO	YES	YES	YES	NO	III	III
22	JLO	984847	58	YES	NO	NO	NO	YES	NO	YES	NO	III	III
23	SK	314517	59	NO	YES	NO	NO	YES	NO	NO	NO	II	I
24	PM	929889	63	NO	NO	YES	NO	NO	YES	YES	NO	III	II
25	DK	1520440	54	NO	YES	NO	NO	NO	YES	YES	NO	III	II
26	LA	1681977	62	NO	YES	NO	NO	YES	YES	NO	NO	II	I
27	JK	1681578	63	YES	NO	NO	NO	YES	NO	NO	NO	III	III
28	Ap	1669364	60	NO	NO	NO	YES	NO	YES	YES	NO	III	III
29	JK	911508	54	YES	YES	NO	NO	YES	NO	NO	YES	II	I
30	NR	167480	52	NO	YES	NO	NO	YES	NO	NO	NO	II	II
31	SK	1554714	56	NO	YES	NO	NO	NO	YES	YES	NO	III	I
32	DS	196914	52	NO	YES	NO	NO	YES	YES	NO	NO	II	III
33	HP	1677988	56	NO	YES	NO	NO	NO	YES	NO	NO	II	III
34	KG	699280	54	NO	YES	NO	NO	YES	NO	YES	NO	III	I
35	SR	1680744	58	NO	NO	NO	NO	NO	YES	NO	NO	II	I
36	MK	262519	64	NO	YES	NO	NO	YES	YES	YES	NO	III	I
37	DR	224415	58	NO	YES	NO	NO	YES	NO	NO	NO	II	III
38	TS	1694338	55	NO	YES	NO	NO	NO	YES	YES	NO	III	II
39	N	1660914	61	NO	NO	NO	NO	YES	YES	NO	NO	II	I
40	HK	1663879	52	NO	NO	NO	NO	YES	YES	NO	NO	II	II
41	S	1721813	48	YES	NO	NO	YES	NO	NO	YES	NO	III	II
42	DJ	1719764	36	NO	YES	NO	NO	YES	YES	NO	NO	II	III
43	RK	1396643	46	NO	YES	NO	NO	NO	NO	NO	NO	II	II
44	BKG	1713015	48	YES	NO	NO	YES	NO	NO	NO	YES	II	I

SR NO	Initials	MRD	PHENOTYPE	AGE	AGE GROUP	SEX	SBP	DBP	PR	BMI	BMI GROUP	ALCOHOLIC	SMOKER	DM	HTN	CAD	REVASCULARISATION
45	RK	1381693	B	78	2	M	128	76	76	32	5	NO	NO	NO	YES	NO	NO
46	SD	169398	B	62	1	F	130	76	116	27	4	NO	NO	YES	YES	NO	NO
47	LD	265710	B	70	2	F	156	64	76	29	4	NO	NO	NO	YES	NO	NO
48	GG	1735323	B	74	2	F	110	70	84	24	3	NO	NO	NO	YES	NO	NO
49	BJ	846334	B	69	2	F	142	88	60	26	4	NO	NO	NO	YES	YES	YES
50	BKG	1740003	B	59	1	F	160	70	72	32	5	NO	NO	YES	YES	NO	NO
51	HK	1754020	B	69	2	F	128	88	90	27	4	NO	NO	NO	YES	NO	NO
52	SJ	1710760	B	60	1	M	120	56	87	22	2	NO	YES	NO	YES	NO	NO
53	KK	1661094	B	66	2	M	140	56	65	28	4	NO	NO	YES	YES	YES	NO
54	KK	260520	B	68	2	F	122	56	85	32	5	NO	NO	NO	YES	NO	NO
55	SB	1677200	B	68	2	F	108	60	68	35	5	NO	NO	YES	YES	NO	NO
56	ML	196800	B	61	1	M	144	70	72	29	4	YES	NO	YES	YES	YES	YES
57	SB	1554776	B	67	2	F	118	78	76	28	4	NO	NO	NO	YES	NO	NO
58	SB	262480	B	63	1	F	146	90	90	26	4	NO	NO	YES	YES	NO	NO
59	VP	1721840	B	62	1	M	150	90	88	35	5	YES	NO	NO	YES	YES	NO
60	SD	250430	B	61	1	F	120	56	76	32	5	NO	NO	YES	YES	NO	NO
61	GK	178435	B	60	1	M	136	72	83	32	5	YES	YES	YES	YES	YES	YES
62	SK	1714433	B	65	2	M	150	90	68	35	5	NO	NO	NO	YES	NO	NO
63	SK	1721844	B	62	1	F	130	70	76	34	5	NO	NO	YES	YES	NO	NO
64	RK	1683465	B	72	2	F	128	78	70	36	5	NO	NO	NO	YES	NO	NO
65	JK	266733	B	63	1	M	130	84	75	37	5	NO	NO	NO	YES	YES	NO
66	SS	846434	B	70	2	M	130	90	96	29	4	NO	NO	NO	YES	NO	NO
67	JS	254634	B	69	2	M	126	80	72	20	2	NO	NO	YES	YES	NO	NO
68	SK	65758	B	62	1	F	140	78	91	34	5	NO	NO	NO	YES	NO	NO
69	RK	654356	B	59	1	M	128	68	87	24	3	NO	NO	NO	YES	NO	NO
70	SD	126789	B	64	1	F	130	76	80	29	4	NO	NO	NO	YES	NO	NO
71	K	1732455	B	68	2	F	110	70	75	24	3	NO	NO	NO	NO	NO	NO
72	JK	546778	B	67	2	F	156	92	70	27	4	NO	NO	NO	YES	NO	NO
73	H	123980	B	61	1	F	118	78	66	28	4	NO	NO	YES	YES	NO	NO
74	S	654789	B	66	2	F	126	76	84	26	4	NO	NO	YES	YES	NO	NO
75	K	1743567	B	65	2	F	140	70	80	27	4	NO	NO	YES	YES	NO	NO
76	SK	65478	B	64	1	F	130	76	92	29	4	NO	NO	NO	YES	NO	NO
77	GA	4887	B	68	2	M	128	78	65	21	2	YES	NO	YES	YES	NO	NO
78	PK	1678549	B	58	1	F	108	66	73	28	4	NO	NO	YES	YES	YES	YES
79	SK	143456	B	68	2	F	140	88	88	28	4	NO	NO	NO	YES	YES	NO
80	KK	1745678	B	59	1	F	130	66	72	29	4	NO	NO	YES	NO	NO	NO
81	A	324566	B	60	1	F	118	90	78	25	4	NO	NO	NO	YES	YES	YES
82	LD	56748	B	59	1	F	160	92	69	21	2	NO	NO	YES	YES	NO	NO
83	S	1765890	B	76	2	F	138	90	80	28	4	NO	NO	NO	YES	YES	YES
84	SS	1643578	B	69	2	F	126	98	90	29	4	NO	NO	NO	YES	NO	NO
85	LD	1678324	B	68	2	F	120	90	71	24	3	NO	NO	YES	YES	NO	NO
86	RK	1683456	B	60	1	F	118	98	65	26	4	NO	NO	YES	YES	YES	NO
87	PD	1578343	B	67	2	F	116	90	74	27	4	NO	NO	YES	YES	YES	NO
88	DK	5678	B	58	1	F	128	88	63	20	2	NO	NO	YES	YES	N	NO

SR NO	Initials	MRD	AF	HYPOTHYROID	HB	creatinine	NTPROBNP	EF	MITAL E	MITRAL A	E/A	E/E'	LA size	TR	DD	6 MWT
45	RK	1381693	NO	NO	13.4	1	1438	60	61	93	0.7	27	44	44	3	280
46	SD	169398	YES	YES	11.2	0.7	1010	60	88	0		22	50	38	2	240
47	LD	265710	YES	NO	9.8	0.9	1800	60	56	85	0.6	22	42	36	3	200
48	GG	1735323	NO	YES	11.4	0.9	2442	60	95	63	1.4	19	31	32	2	230
49	BJ	846334	NO	NO	12.8	0.6	2040	60	95	63	1.4	19	31	42	2	200
50	BKG	1740003	NO	NO	10.5	0.8	1560	60	122	34	3.6	20	43	45	2	170
51	HK	1754020	NO	NO	10.2	0.8	1386	60	60	50	1.2	18	48	36	2	150
52	SJ	1710760	NO	NO	14	0.9	1448	55	65	132	0.5	26	44	28	3	230
53	KK	1661094	NO	NO	12.9	0.5	1033	60	150	119	1.2	24	45	32	1	180
54	KK	260520	YES	NO	11.7	0.3	1446	60	141	123	1.1	28	48	30	1	234
55	SB	1677200	NO	NO	11	1	1268	56	70	121	0.6	16.5	43	48	2	404
56	ML	196800	NO	NO	12	0.87	1626	60	96	64	1.4	24	34	22	2	380
57	SB	1554776	NO	NO	13.7	0.6	1250	60	70	107	0.6	24	27	44	2	188
58	SB	262480	NO	NO	10.9	0.8	2070	60	119	112	1.1	22	34	38	3	414
59	VP	1721840	NO	NO	13.4	0.9	2054	60	69	116	0.6	16	43	36	2	480
60	SD	250430	NO	NO	12	0.5	2014	60	142	123	1.1	18	52	32	3	150
61	GK	178435	NO	NO	11.5	0.68	2380	60	131	127	1	20.5	42	42	1	390
62	SK	1714433	NO	NO	12.8	1	1817	60	83	60	1.4	16.7	46	45	1	250
63	SK	1721844	YES	NO	14	0.8	1460	60	88	0		18	39	36	2	190
64	RK	1683465	YES	NO	11	0.5	1356	60	80	0		16.5	34	28	3	480
65	JK	266733	NO	NO	13.2	1.1	2084	50	55	93	0.6	15.4	34	32	1	460
66	SS	846434	NO	NO	14	0.8	1438	60	88	111	0.7	15.6	42	30	2	378
67	JS	254634	YES	NO	11.7	0.5	1878	60	123	0		20	55	30	3	276
68	SK	65758	YES	NO	9.6	0.7	1400	60	153	0		18	35	30	1	130
69	RK	654356	NO	NO	10.1	1.1	1760	60	79	83	0.9	14	46	30	1	266
70	SD	126789	NO	NO	14	1.1	1480	60	75	67	0.8	19.5	45	50	2	270
71	K	1732455	YES	NO	10.7	0.6	1796	60	142	0		17.5	51	24	2	444
72	JK	546778	NO	NO	12.1	0.9	2332	60	132	140	0.8	24	32	40	2	186
73	H	123980	NO	NO	12.3	1	1342	60	97	129	0.7	15.2	34	28	1	378
74	S	654789	NO	NO	12.9	1	2248	60	100	110	0.9	14	41	44	1	466
75	K	1743567	NO	NO	13.7	1	2129	60	57	108	0.5	18.7	34	38	1	480
76	SK	65478	NO	NO	14.4	0.87	2272	60	77	77	1	14.6	42	36	1	278
77	GA	4887	NO	NO	11	1.1	2222	60	84	72	1.2	22	34	32	3	346
78	PK	1678549	NO	NO	13.6	1	2358	60	83	54	1.5	10.4	40	42	2	438
79	SK	143456	NO	NO	11.6	0.84	1702	60	85	88	0.9	16	43	45	3	246
80	KK	1745678	NO	NO	13	0.7	1823	60	72	68	1.1	20	29	36	1	422
81	A	324566	NO	NO	10.9	0.8	1664	60	133	113	1.2	23	44	28	1	86
82	LD	56748	NO	NO	15	0.6	1744	60	97	82	0.6	14	34	32	1	490
83	S	1765890	YES	NO	12	0.3	1827	60	68	0		32	45	30	3	110
84	SS	1643578	NO	NO	13.2	0.3	1566	60	94	106	0.9	19.8	34	30	1	328
85	LD	1678324	NO	NO	12.4	1	1842	60	91	103	0.9	17.7	42	28	2	252
86	RK	1683456	NO	NO	10.8	1	1942	60	66	82	0.8	19	39	30	2	178
87	PD	1578343	NO	NO	14.3	0.8	1980	60	134	53	1.2	34.6	36	50	3	242
88	DK	5678	NO	NO	11.7	1	2068	60	125	127	1	20	52	32	1	78

SR NO	Initials	MRD	KCCQ	ACEI	ARB	ARNI	SGLT2	DIURETICS	MRA	No. of hospitalization due to heart failure DURING FOLLOW UP	Mortality	NYHA CLASS	NYHA CLASS LAST FOLLOW UP
45	RK	1381693	50	NO	NO	NO	YES	NO	YES	YES	NO	III	I
46	SD	169398	54	NO	YES	NO	YES	YES	NO	NO	NO	II	I
47	LD	265710	52	NO	YES	NO	NO	YES	NO	NO	NO	II	III
48	GG	1735323	54	YES	NO	NO	NO	YES	NO	YES	NO	III	II
49	BJ	846334	44	NO	YES	NO	NO	YES	YES	NO	NO	II	I
50	BKG	1740003	49	NO	YES	NO	YES	YES	NO	NO	NO	III	III
51	HK	1754020	48	NO	NO	NO	NO	YES	NO	YES	NO	III	III
52	SJ	1710760	46	NO	NO	NO	NO	YES	NO	NO	NO	II	III
53	KK	1661094	54	YES	NO	NO	NO	NO	NO	NO	NO	II	III
54	KK	260520	48	NO	YES	NO	NO	YES	YES	NO	NO	II	II
55	SB	1677200	48	NO	NO	NO	YES	YES	NO	NO	NO	II	II
56	ML	196800	50	NO	NO	NO	YES	NO	NO	YES	NO	III	II
57	SB	1554776	56	YES	NO	NO	NO	NO	NO	NO	NO	II	III
58	SB	262480	52	NO	NO	NO	NO	NO	YES	NO	NO	II	II
59	VP	1721840	52	NO	NO	NO	NO	NO	NO	YES	NO	III	III
60	SD	250430	48	NO	NO	NO	NO	YES	YES	NO	NO	II	II
61	GK	178435	48	YES	YES	NO	YES	YES	NO	NO	NO	II	II
62	SK	1714433	50	NO	YES	NO	NO	NO	NO	YES	NO	III	III
63	SK	1721844	50	NO	YES	NO	YES	YES	NO	NO	NO	II	II
64	RK	1683465	52	NO	YES	NO	NO	NO	NO	NO	NO	II	III
65	JK	266733	50	YES	YES	NO	NO	NO	NO	YES	YES	III	I
66	SS	846434	54	NO	YES	NO	NO	NO	YES	NO	NO	II	II
67	JS	254634	50	NO	YES	NO	YES	NO	NO	NO	NO	II	II
68	SK	65758	54	NO	NO	NO	NO	YES	YES	YES	NO	III	III
69	RK	654356	48	YES	YES	NO	NO	NO	NO	YES	NO	III	III
70	SD	126789	48	NO	YES	NO	NO	NO	NO	NO	NO	II	III
71	K	1732455	54	NO	NO	NO	NO	NO	NO	NO	NO	II	III
72	JK	546778	46	NO	YES	NO	NO	NO	NO	NO	NO	II	III
73	H	123980	52	NO	YES	NO	YES	NO	NO	YES	NO	III	III
74	S	654789	54	YES	YES	NO	YES	YES	YES	NO	NO	II	II
75	K	1743567	54	NO	YES	NO	NO	NO	NO	NO	NO	II	III
76	SK	65478	52	NO	YES	NO	NO	NO	NO	NO	NO	II	III
77	GA	4887	48	NO	NO	NO	YES	YES	NO	NO	NO	II	II
78	PK	1678549	46	YES	YES	NO	NO	NO	YES	NO	NO	II	II
79	SK	143456	48	NO	YES	NO	NO	NO	NO	NO	NO	II	III
80	KK	1745678	50	NO	NO	NO	NO	NO	NO	YES	NO	III	III
81	A	324566	45	NO	YES	NO	NO	NO	YES	NO	NO	II	III
82	LD	56748	55	YES	YES	NO	YES	NO	NO	NO	NO	II	II
83	S	1765890	54	NO	NO	NO	YES	YES	YES	NO	NO	II	II
84	SS	1643578	46	NO	YES	NO	NO	NO	YES	NO	NO	II	II
85	LD	1678324	44	YES	NO	NO	NO	YES	NO	YES	NO	III	III
86	RK	1683456	49	NO	YES	NO	YES	NO	NO	NO	NO	II	II
87	PD	1578343	41	NO	YES	NO	NO	YES	NO	NO	NO	II	II
88	DK	5678	54	NO	YES	NO	YES	YES	YES	NO	YES	III	I

SR NO	Initials	MRD	PHENOTYPE	AGE	AGE GROUP	SEX	SBP	DBP	PR	BMI	BMI GROUP	ALCOHOLIC	SMOKER	DM	HTN	CAD	REVASCULARISATION
89	M	17324598	B	69	2	F	148	90	67	27	4	NO	NO	NO	YES	N	NO
90	AK	1714356	B	67	2	F	154	76	90	29	4	NO	NO	NO	YES	YES	NO
91	A	1743567	B	60	1	F	130	74	96	23	3	NO	NO	NO	YES	N	NO
92	GA	1798435	B	61	1	F	120	66	82	23	3	YES	NO	NO	YES	YES	NO
93	AK	1643570	B	68	2	F	128	84	75	34	5	NO	YES	NO	YES	YES	NO
94	S	1644487	B	62	1	F	106	74	96	28	4	NO	NO	YES	YES	YES	NO
95	T	1788888	B	60	1	F	148	96	76	20	2	NO	NO	YES	YES	YES	YES
96	AK	1657890	B	61	1	F	110	66	80	20	2	YES	YES	NO	YES	YES	NO
97	JK	1765894	B	76	2	F	130	66	90	27	4	NO	NO	YES	YES	N	NO
98	HK	1734560	B	62	1	F	140	90	84	27	4	NO	NO	YES	YES	YES	NO
99	A	1684393	B	70	2	F	156	90	78	28	4	YES	NO	YES	YES	YES	NO
100	P	1657890	B	72	2	F	128	66	65	28	4	NO	YES	NO	YES	N	NO
101	P	1768904	B	64	1	F	120	76	80	24	3	NO	NO	YES	YES	YES	YES
102	P	1456677	B	64	1	F	142	85	70	24	3	NO	NO	NO	YES	YES	NO
103	RD	1547894	B	72	2	F	160	70	70	27	4	NO	NO	NO	YES	N	NO
104	S	1854678	B	63	1	F	150	80	66	19	2	NO	NO	NO	YES	YES	NO
105	M	5467	B	62	1	F	130	90	74	18	1	NO	NO	NO	YES	YES	NO
106	HK	1396240	B	68	2	F	110	77	60	24	3	NO	NO	NO	YES	N	NO
107	BK	1616148	B	60	1	F	120	78	80	27	4	NO	NO	NO	YES	YES	NO
108	HK	1180388	B	62	1	F	130	80	78	28	4	NO	NO	NO	NO	YES	YES
109	RV	1233788	B	66	2	F	140	70	70	24	3	YES	NO	YES	YES	N	NO
110	SR	1700750	B	65	2	F	130	70	94	27	4	YES	NO	NO	YES	YES	NO
111	SD	1725809	B	66	2	F	120	60	84	24	3	NO	NO	YES	YES	YES	NO
112	RK	1511973	B	64	1	F	130	80	68	24	3	NO	NO	NO	YES	YES	NO
113	AK	973506	B	68	2	F	138	78	68	24	3	NO	NO	NO	YES	YES	NO
114	RS	1765524	B	76	2	F	140	70	74	21	2	NO	NO	NO	YES	YES	NO
115	SK	1741462	B	65	2	F	130	90	84	20	2	NO	NO	NO	YES	YES	NO
116	R	1408530	B	70	2	F	140	90	86	28	4	NO	NO	NO	YES	YES	NO
117	TK	1734234	B	74	2	F	140	90	72	24	3	NO	NO	NO	YES	YES	NO
118	SK	1336636	B	65	2	F	134	90	78	27	4	NO	NO	NO	YES	YES	NO
119	RK	1785363	B	66	2	F	150	90	64	28	4	NO	NO	NO	YES	YES	NO
120	SR	165780	B	62	1	F	140	90	72	24	3	NO	NO	NO	YES	NO	NO
121	R	1728271	B	64	1	F	150	70	68	24	3	NO	NO	NO	YES	YES	NO
122	RK	134168	B	68	2	F	150	80	68	21	2	NO	YES	NO	YES	YES	NO
123	RK	1761095	B	65	2	F	140	70	82	20	2	NO	NO	NO	YES	YES	NO
124	V	174849	B	76	2	F	148	82	74	23	3	NO	NO	NO	YES	NO	NO
125	MK	1602499	B	61	1	F	100	70	74	27	4	YES	YES	NO	NO	YES	NO
126	JK	1617835	B	60	1	F	140	70	50	24	3	NO	NO	NO	YES	YES	NO
127	AR	715733	B	79	2	F	100	70	78	28	4	NO	NO	NO	NO	YES	NO
128	BS	1734927	B	63	1	F	130	90	76	24	3	NO	NO	YES	YES	YES	NO
129	HK	1360919	B	64	1	F	150	82	82	27	4	NO	NO	YES	YES	YES	NO
130	KP	1628757	B	65	2	F	184	78	78	22	2	NO	NO	YES	YES	YES	NO
131	TK	106194	B	60	1	F	158	84	84	22	2	NO	NO	YES	YES	YES	NO
132	KM	147313	B	69	2	F	126	74	78	27	4	NO	NO	YES	YES	YES	NO

SR NO	Initials	MRD	AF	HYPOTHYROID	HB	creatinine	NTPROBNP	EF	MITAL E	MITRAL A	E/A	E/E'	LA size	TR	DD	6 MWT
89	M	17324598	NO	NO	10.9	1.2	1678	60	101	58	1.7	17.8	44	42	1	456
90	AK	1714356	NO	NO	12	0.9	1836	60	60	110	0.5	22	39	45	2	164
91	A	1743567	YES	NO	9.9	1	1834	60	107	0		20	49	36	2	398
92	GA	1798435	NO	NO	12.3	0.6	1730	60	84	108	0.8	13.1	40	28	2	230
93	AK	1643570	NO	NO	10.6	0.8	2070	60	106	126	0.8	22	46	32	1	110
94	S	1644487	NO	NO	10	0.5	1803	60	130	58	2.2	28	44	30	1	156
95	T	1788888	NO	NO	12.5	0.7	1832	60	104	98	1	32	34	30	3	198
96	AK	1657890	NO	NO	13.9	0.9	1878	60	128	112	1.1	18.9	52	30	2	368
97	JK	1765894	NO	NO	14.6	0.7	1544	54	94	106	0.9	19.8	38	30	2	440
98	HK	1734560	NO	NO	12.4	1	1822	60	55	63	0.8	34	36	50	2	458
99	A	1684393	NO	NO	13.9	0.3	1688	60	56	81	0.7	14	37	24	1	220
100	P	1657890	NO	NO	15	2.6	1932	50	104	82	1.3	18	36	40	3	122
101	P	1768904	NO	NO	11.8	2.9	1920	60	76	76	1	14.6	42	28	1	270
102	P	1456677	NO	NO	13.2	2.1	1856	60	98	80	1.1	14.58	46	42	1	330
103	RD	1547894	NO	NO	11.2	2.8	1788	60	90	130	0.7	24	50	34	2	270
104	S	1854678	YES	NO	12.1	2	1866	60	68	0	0.8	20	36	36	3	240
105	M	5467	YES	YES	12.6	0.6	1740	60	56	42	1.2	10.7	41	32	1	270
106	HK	1396240	YES	NO	11.7	0.9	1988	60	68	40	1	14	48	42	1	150
107	BK	1616148	NO	NO	12.3	0.81	1832	55	89	108	0.88	14.8	29	34	3	210
108	HK	1180388	NO	YES	12.2	2.8	1976	60	0.9	1.01	0.89	0.13	35	36	2	240
109	RV	1233788	YES	YES	11.4	3.2	1910	60	0.56	0.73	0.7	23	39	32	2	180
110	SR	1700750	NO	NO	12	2.5	1856	60	76	76	1	15	42	36	2	240
111	SD	1725809	YES	NO	10.2	1.2	2602	60	116	112	1	16	40	42	3	360
112	RK	1511973	YES	NO	10.9	1.1	1840	60	116	82	1.2	18	33	38	2	120
113	AK	973506	NO	YES	12	0.8	1940	60	55	63	0.8	34	36	24	2	372
114	RS	1765524	NO	NO	10.3	1	1840	60	128	110	0.2	20	52	40	2	480
115	SK	1741462	YES	NO	13	2.6	1754	60	81	93.8	0.9	8	33	28	3	120
116	R	1408530	NO	YES	12	2.3	1822	60	52	73	0.7	5	38	42	2	330
117	TK	1734234	YES	NO	12.3	3.1	1903	48	98	80	1.2	22	46	34	1	240
118	SK	1336636	NO	NO	12.9	1	2150	60	7	6	1.13	14	43	36	2	90
119	RK	1785363	NO	NO	13.1	2.7	1980	60	7	9	0.7	11	34	42	3	270
120	SR	165780	YES	YES	13.9	0.6	1970	60	8	7	1.15	16	42	40	1	210
121	R	1728271	NO	NO	9.8	0.6	1874	60	9	7	1.8	1.15	45	38	2	180
122	RK	134168	NO	NO	12	0.6	1947	60	10	7	1.4	11.4	45	24	3	310
123	RK	1761095	YES	NO	12	0.7	1540	60	7	12	0.9	13	40	40	2	210
124	V	174849	NO	NO	13	2.8	1490	60	6	9	0.6	14.5	45	28	3	90
125	MK	1602499	NO	NO	13.9	2.3	1530	60	7.2	8.1	0.9	7.24	28	42	2	170
126	JK	1617835	NO	NO	11.8	2.9	2190	60	94	75	1.2	18.1	48	36	2	80
127	AR	715733	YES	YES	12.8	2.8	1650	60	70	92	0.76	22	34	40	2	220
128	BS	1734927	NO	NO	13.9	2.1	1920	60	70	70	1	9.1	34	31	3	320
129	HK	1360919	NO	NO	12	2.7	2120	60	78	97	0.8	12.6	34	36	1	320
130	KP	1628757	YES	NO	13.4	3.1	1434	60	93	88	1	18	35	42	2	240
131	TK	106194	NO	NO	13.5	2.5	2407	60	84	100	0.8	11	30	36	2	280
132	KM	147313	NO	NO	11.7	1.9	1630	60	74	84	0.8	12	42	40	3	320

SR NO	Initials	MRD	KCCQ	ACEI	ARB	ARNI	SGLT2	DIURETICS	MRA	No. of hospitalization due to heart failure DURING FOLLOW UP	Mortality	NYHA CLASS	NYHA CLASS LAST FOLLOW UP
89	M	17324598	53	YES	NO	NO	NO	YES	NO	NO	NO	II	II
90	AK	1714356	47	NO	YES	NO	NO	YES	NO	NO	NO	II	II
91	A	1743567	52	NO	YES	NO	NO	YES	NO	NO	NO	II	II
92	GA	1798435	49	YES	YES	NO	NO	NO	YES	YES	NO	III	II
93	AK	1643570	55	NO	YES	NO	YES	NO	NO	NO	NO	II	III
94	S	1644487	48	NO	YES	NO	NO	YES	NO	NO	NO	II	II
95	T	1788888	51	YES	YES	NO	YES	NO	YES	NO	NO	III	II
96	AK	1657890	45	NO	YES	NO	NO	NO	NO	NO	NO	II	II
97	JK	1765894	53	YES	YES	NO	NO	NO	YES	NO	NO	II	II
98	HK	1734560	49	NO	YES	NO	YES	NO	NO	NO	NO	II	II
99	A	1684393	48	YES	YES	NO	NO	NO	YES	YES	NO	III	III
100	P	1657890	45	NO	NO	NO	NO	YES	NO	NO	NO	II	II
101	P	1768904	47	YES	YES	NO	NO	YES	YES	NO	NO	II	II
102	P	1456677	46	NO	NO	NO	NO	YES	YES	NO	NO	II	II
103	RD	1547894	47	YES	YES	NO	NO	YES	NO	NO	NO	II	II
104	S	1854678	45	NO	NO	NO	NO	YES	NO	NO	NO	II	II
105	M	5467	54	NO	YES	NO	NO	YES	NO	NO	NO	II	II
106	HK	1396240	49	NO	NO	NO	NO	YES	YES	NO	NO	II	II
107	BK	1616148	48	YES	NO	NO	NO	YES	YES	YES	NO	III	II
108	HK	1180388	47	NO	NO	NO	NO	NO	NO	NO	NO	II	III
109	RV	1233788	51	NO	YES	NO	NO	YES	NO	YES	NO	III	III
110	SR	1700750	49	NO	YES	NO	NO	NO	NO	NO	NO	II	III
111	SD	1725809	54	YES	NO	NO	NO	YES	NO	YES	NO	III	III
112	RK	1511973	47	NO	NO	NO	NO	NO	YES	NO	YES	II	II
113	AK	973506	48	NO	YES	NO	NO	NO	NO	NO	NO	II	II
114	RS	1765524	46	YES	NO	NO	NO	NO	NO	NO	NO	II	III
115	SK	1741462	47	NO	YES	NO	NO	NO	YES	YES	NO	III	III
116	R	1408530	46	NO	NO	NO	NO	YES	NO	NO	NO	II	II
117	TK	1734234	50	YES	NO	NO	NO	YES	NO	NO	NO	II	II
118	SK	1336636	44	NO	NO	NO	NO	YES	NO	NO	NO	II	II
119	RK	1785363	50	NO	NO	NO	NO	NO	YES	YES	NO	III	III
120	SR	165780	49	NO	YES	NO	NO	YES	NO	NO	NO	II	II
121	R	1728271	48	YES	YES	NO	NO	NO	YES	NO	NO	II	III
122	RK	134168	46	NO	YES	NO	NO	NO	YES	NO	NO	II	II
123	RK	1761095	53	YES	NO	NO	NO	YES	NO	NO	NO	II	II
124	V	174849	48	NO	YES	NO	NO	NO	NO	YES	NO	III	IV
125	MK	1602499	54	NO	NO	NO	NO	YES	NO	NO	NO	II	II
126	JK	1617835	52	YES	YES	NO	NO	YES	YES	NO	NO	II	II
127	AR	715733	47	NO	NO	NO	YES	YES	NO	NO	NO	II	II
128	BS	1734927	47	NO	YES	NO	NO	YES	NO	YES	NO	III	III
129	HK	1360919	49	NO	YES	NO	NO	NO	YES	NO	NO	II	II
130	KP	1628757	50	YES	NO	NO	NO	YES	NO	NO	NO	II	II
131	TK	106194	52	NO	YES	NO	NO	YES	NO	NO	NO	II	III
132	KM	147313	45	NO	NO	NO	NO	YES	YES	NO	NO	II	III

SR NO	Initials	MRD	PHENOTYPE	AGE	AGE GROUP	SEX	SBP	DBP	PR	BMI	BMI GROUP	ALCOHOLIC	SMOKER	DM	HTN	CAD	REVASCULARISATION
133	SK	636999	B	65	2	F	132	88	86	24	3	NO	NO	YES	YES	YES	NO
134	RK	1787524	B	76	2	F	134	74	68	24	3	NO	NO	YES	YES	YES	NO
135	J	1744823	B	72	2	F	150	86	80	28	4	NO	NO	YES	NO	YES	NO
136	RC	1243080	B	68	2	F	144	82	72	27	4	NO	NO	YES	YES	YES	NO
137	BSG	1522542	B	66	2	F	104	68	84	28	4	NO	NO	YES	YES	YES	NO
138	V	498314	B	64	1	F	130	86	70	27	4	NO	NO	YES	YES	YES	NO
139	LS	105655	C	46	1	M	132	70	76	20	2	NO	NO	YES	YES	YES	YES
140	RV	1170457	C	44	1	F	146	86	76	21	2	NO	NO	YES	YES	YES	NO
141	CK	196145	C	57	1	M	136	88	88	23	3	NO	NO	YES	YES	YES	YES
142	S	1755234	C	40	1	M	130	66	58	24	3	NO	NO	NO	YES	YES	NO
143	MK	1761296	C	42	1	M	120	70	86	32	5	NO	NO	NO	YES	YES	NO
144	MK	557201	C	42	1	M	120	84	64	20	2	NO	NO	NO	YES	YES	YES
145	KL	1761957	C	51	1	M	124	76	48	20	2	NO	NO	NO	YES	YES	NO
146	LJ	198729	C	43	1	M	146	86	76	24	3	NO	NO	NO	NO	YES	YES
147	SM	1777907	C	52	1	M	130	70	92	26	4	NO	YES	NO	NO	YES	NO
148	GK	1756015	C	50	1	F	130	78	80	24	3	NO	NO	NO	YES	YES	NO
149	PL	1773852	C	48	1	F	132	80	94	26	4	NO	NO	YES	NO	NO	NO
150	AR	1345529	C	40	1	M	150	100	90	20	2	NO	NO	YES	YES	YES	NO
151	PG	1783609	C	42	1	M	130	88	62	26	4	NO	NO	YES	YES	YES	YES
152	MB	1277363	C	42	1	M	120	70	80	20	2	NO	NO	YES	NO	NO	NO
153	PKK	1012149	C	45	1	M	130	76	72	21	2	YES	NO	NO	NO	NO	NO
154	AK	200470	C	56	1	M	140	86	68	23	3	NO	NO	NO	YES	YES	YES
155	KK	182535	C	50	1	M	142	80	52	26	4	NO	NO	NO	YES	NO	NO
156	PK	455385	C	51	1	F	140	96	90	24	3	NO	NO	NO	NO	YES	NO
157	SG	158731	C	44	1	M	130	74	66	24	3	NO	NO	NO	YES	NO	NO
158	JK	119188	C	43	1	F	124	60	64	29	4	NO	NO	YES	NO	YES	YES
159	SS	1497254	C	47	1	M	108	54	98	28	4	NO	NO	YES	YES	YES	NO
160	R	1616233	C	37	1	M	140	90	94	29	4	NO	NO	NO	NO	NO	NO
161	JK	1033821	C	32	1	M	110	80	74	32	5	NO	NO	NO	YES	YES	YES
162	KK	1438537	C	40	1	M	140	70	72	23	3	NO	NO	NO	NO	NO	NO
163	HK	1488171	C	49	1	M	122	82	86	21	2	NO	NO	NO	YES	YES	NO
164	A	256866	C	46	1	M	114	65	64	26	4	NO	NO	NO	NO	YES	NO
165	PS	1625060	C	45	1	M	130	86	80	26	4	NO	NO	NO	NO	YES	NO
166	R	1562089	C	55	1	M	118	74	70	26	4	NO	NO	NO	NO	YES	NO
167	RO	1590396	C	50	1	M	128	98	70	24	3	NO	NO	NO	YES	YES	NO
168	PK	287181	C	40	1	M	138	74	86	24	3	NO	NO	NO	YES	NO	NO
169	RR	1138924	C	48	1	F	112	66	86	29	4	NO	NO	NO	NO	NO	NO
170	SJ	205769	C	43	1	M	120	70	78	23	3	NO	NO	NO	YES	YES	NO
171	SS	1532321	C	42	1	M	112	76	90	23	3	NO	NO	NO	NO	NO	NO
172	CLC	1614402	C	44	1	F	128	74	50	24	3	NO	NO	NO	YES	YES	NO
173	RKD	164092	C	48	1	M	150	94	66	29	4	NO	YES	NO	YES	YES	NO
174	BS	1392357	C	40	1	M	140	92	76	32	5	NO	NO	NO	NO	YES	NO
175	KK	987459	C	40	1	F	160	86	70	21	2	NO	NO	NO	NO	NO	NO

SR NO	Initials	MRD	AF	HYPOTHYROID	HB	creatinine	NTPROBNP	EF	MITAL E	MITRAL A	E/A	E/E'	LA size	TR	DD	6 MWT
133	SK	636999	YES	NO	13.4	2.8	1666	60	82	76	1.08	18	34	31	3	200
134	RK	1787524	NO	NO	12.3	3.2	2460	60	102	54	1.9	16	51	36	2	320
135	J	1744823	NO	YES	11.4	2.3	1635	60	98	87	1.1	16	45	42	2	240
136	RC	1243080	NO	NO	9.6	1.3	1662	60	78	112	0.6	18	41	33	3	140
137	BSG	1522542	YES	NO	12	2.6	1935	60	117	0		15	47	41	3	170
138	V	498314	NO	NO	11	2.8	1610	60	175	52	3.3	36	45	33	2	210
139	LS	105655	NO	NO	13.2	3.2	1340	60	65	73	0.8	15	42	36	2	266
140	RV	1170457	NO	NO	13.9	0.9	1226	60	57	98	0.5	16	40	50	3	240
141	CK	196145	NO	NO	12.8	0.2	1442	60	93	88	1.1	20	36	45	2	400
142	S	1755234	YES	NO	12.2	0.9	1420	60	65	0	0	16	42	40	3	248
143	MK	1761296	NO	NO	11.1	0.4	1766	60	146	77	1.9	27	42	31	1	266
144	MK	557201	NO	NO	11	0.2	1150	60	81	75	1	12	42	36	1	360
145	KL	1761957	NO	NO	13.3	0.6	1302	60	118	121	1	26	56	42	3	206
146	LJ	198729	YES	NO	11.3	2.3	1760	60	62	89	0.6	15	44	40	2	280
147	SM	1777907	NO	NO	13.2	2.1	1560	60	158	132	1.2	18	44	34	1	320
148	GK	1756015	NO	NO	13	2.3	1220	60	55	74	0.8	7.1	34	44	2	250
149	PL	1773852	NO	NO	12.4	0.6	1547	60	102	91	1.1	22	42	42	1	220
150	AR	1345529	YES	NO	13	1	1765	60	51	91	0.5	10	44	46	3	380
151	PG	1783609	NO	NO	9.2	0.9	1546	60	95	95	1	18	44	40	2	260
152	MB	1277363	NO	NO	10.4	1.3	1730	60	114	83	1.3	16	42	30	1	240
153	PKK	1012149	NO	NO	11.6	0.9	1220	60	54	66	0.8	18	46	32	2	400
154	AK	200470	NO	NO	14.1	0.9	1338	60	106	58	1.8	17	42	40	2	240
155	KK	182535	NO	NO	12.6	0.6	1418	60	110	78	1.4	14	44	32	1	340
156	PK	455385	YES	NO	9.4	1.8	1470	60	144	140	1	20	55	50	1	344
157	SG	158731	NO	NO	11.7	0.67	1282	60	103	87	1.2	22	53	32	1	320
158	JK	119188	NO	NO	10.8	0.9	1080	60	110	90	0.8	16	45	36	2	324
159	SS	1497254	NO	NO	10.2	0.9	1340	60	148	4	24	22	44	32	2	240
160	R	1616233	YES	NO	12	0.8	1380	60	77	88	0.8	15	44	30	2	308
161	JK	1033821	NO	YES	13	0.6	1630	60	76	54	1.4	14	60	30	1	280
162	KK	1438537	NO	NO	11.5	0.8	1582	60	85	97	0.8		44	30	2	260
163	HK	1488171	NO	NO	9	0.3	1040	60	116	95	1.2	23.2	44	30	1	390
164	A	256866	YES	NO	9.9	0.5	1710	60	115	92	1.2	25	48	50	1	240
165	PS	1625060	NO	NO	11.3	0.9	1350	60	117	51	2.3	30	45	24	3	240
166	R	1562089	YES	NO	13.2	0.8	1550	60	73	60	1.7	17	48	40	2	268
167	RO	1590396	NO	NO	10.9	0.7	1270	60	98	95	1	15	47	28	1	280
168	PK	287181	NO	NO	12.1	0.7	1380	60	67	85	0.7	14	44	32	2	248
169	RR	1138924	YES	NO	11.6	1.2	1294	60	96	54	1.7	14	45	30	3	260
170	SJ	205769	NO	NO	12.7	0.8	1540	60	89	86	1	18	46	40	2	248
171	SS	1532321	NO	NO	11.8	0.9	1330	55	66	94	0.7	14	45	32	2	360
172	CLC	1614402	YES	NO	13.8	0.4	1220	60	98	80	1.2	14	35	40	3	400
173	RKD	164092	NO	NO	14.1	0.6	1304	60	70	100	0.7	18	45	30	1	258
174	BS	1392357	NO	NO	12.1	0.8	1477	60	90	84	1	26	44	32	2	240
175	KK	987459	YES	NO	12.2	0.8	1350	60	83	97	0.9	18	46	40	2	320

SR NO	Initials	MRD	KCCQ	ACEI	ARB	ARNI	SGLT2	DIURETICS	MRA	No. of hospitalization due to heart failure DURING FOLLOW UP	Mortality	NYHA CLASS	NYHA CLASS LAST FOLLOW UP
133	SK	636999	50	NO	NO	NO	NO	NO	NO	NO	YES	III	III
134	RK	1787524	48	NO	YES	NO	NO	NO	NO	NO	NO	II	II
135	J	1744823	47	NO	NO	NO	YES	YES	YES	YES	NO	III	II
136	RC	1243080	48	NO	NO	NO	YES	YES	NO	NO	NO	II	II
137	BSG	1522542	45	NO	NO	NO	NO	YES	NO	NO	NO	II	II
138	V	498314	50	YES	NO	NO	NO	NO	YES	YES	NO	III	IV
139	LS	105655	62	YES	YES	NO	NO	YES	YES	YES	NO	III	IV
140	RV	1170457	65	NO	NO	YES	YES	YES	NO	NO	NO	II	III
141	CK	196145	62	NO	NO	YES	NO	YES	YES	NO	NO	II	I
142	S	1755234	63	NO	NO	YES	NO	YES	NO	NO	NO	II	III
143	MK	1761296	61	NO	NO	YES	YES	NO	NO	NO	NO	II	II
144	MK	557201	59	NO	YES	YES	YES	YES	YES	NO	NO	II	I
145	KL	1761957	62	NO	NO	YES	YES	YES	NO	YES	NO	III	II
146	LJ	198729	61	NO	NO	NO	YES	YES	NO	NO	NO	II	III
147	SM	1777907	63	NO	NO	NO	YES	YES	NO	NO	NO	II	III
148	GK	1756015	65	NO	YES	NO	NO	YES	YES	NO	NO	II	I
149	PL	1773852	60	NO	NO	NO	YES	YES	NO	NO	NO	II	I
150	AR	1345529	60	YES	YES	NO	NO	YES	NO	NO	NO	II	I
151	PG	1783609	57	NO	NO	YES	NO	NO	NO	NO	NO	II	II
152	MB	1277363	62	NO	NO	NO	YES	NO	YES	YES	NO	III	III
153	PKK	1012149	60	NO	NO	NO	YES	NO	NO	NO	NO	II	II
154	AK	200470	63	YES	NO	YES	YES	YES	YES	NO	NO	II	I
155	KK	182535	63	NO	YES	YES	NO	YES	NO	YES	NO	III	III
156	PK	455385	52	NO	NO	NO	NO	YES	NO	NO	NO	II	I
157	SG	158731	63	YES	NO	YES	NO	YES	NO	YES	NO	II	II
158	JK	119188	61	NO	NO	NO	NO	YES	YES	NO	NO	II	I
159	SS	1497254	55	NO	YES	NO	YES	YES	YES	NO	NO	III	III
160	R	1616233	65	NO	NO	NO	YES	YES	NO	NO	NO	III	III
161	JK	1033821	56	YES	NO	YES	NO	YES	NO	YES	NO	III	III
162	KK	1438537	61	NO	NO	NO	NO	YES	NO	NO	NO	II	II
163	HK	1488171	60	YES	NO	YES	YES	YES	YES	NO	NO	III	III
164	A	256866	52	NO	NO	NO	NO	YES	NO	NO	NO	II	III
165	PS	1625060	57	NO	NO	NO	NO	YES	NO	NO	NO	II	I
166	R	1562089	58	NO	NO	NO	NO	NO	NO	NO	NO	II	I
167	RO	1590396	60	YES	YES	NO	YES	YES	NO	NO	NO	II	I
168	PK	287181	57	NO	YES	NO	NO	NO	YES	YES	NO	III	II
169	RR	1138924	64	NO	NO	NO	YES	NO	NO	NO	NO	II	I
170	SJ	205769	63	NO	NO	YES	YES	NO	NO	NO	NO	II	I
171	SS	1532321	59	NO	NO	NO	NO	NO	NO	NO	NO	III	III
172	CLC	1614402	57	YES	NO	YES	YES	NO	YES	NO	NO	II	I
173	RKD	164092	62	YES	YES	YES	NO	NO	NO	NO	NO	II	I
174	BS	1392357	60	NO	NO	NO	NO	NO	NO	NO	NO	II	II
175	KK	987459	58	NO	NO	NO	NO	YES	YES	YES	NO	III	III

Baba Farid University
of Health Sciences
Sadiq Road
Faridkot-151 203 (Pb). INDIA.
Phone : 01639-256232,256236
Tele/Fax : 01639-256235
Email – Thesisbfuhs@gmail.com

75

No. BFUHS/2K23p-TH/ 65 Date 1/1/24

The Principal
Dayanand Medical College & Hospital
Ludhiana

Subject:: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 25.09.2023 has approved the plan of thesis of **Bhoj Raj Sharma**, a student of your college for **DM Cardiology** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
To study different clinical phenotypes and short term follow up in patients presenting with heart failure with preserved ejection fraction .

Supervisor
Dr. Gurpreet S Wander
Prof. & Head
Dept. of Cardiology

Co-Supervisor:-
Dr. Gautam Singal
Asst. Professor
Dept. of Cardiology

The student may submit the thesis in triplicate alongwith the plan in triplicate also, to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She may be directed to attach a photocopy of this letter with the forwarding letter while submitting thesis in the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic, if any.

Controller of Examinations

Note :

1. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*

TO STUDY DIFFERENT CLINICAL PHENOTYPES AND THEIR SHORT TERM FOLLOW UP IN PATIENTS PRESENTING WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

DOCTORATE OF MEDICINE

IN

CARDIOLOGY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES
FARIDKOT

DECEMBER, 2022

DR. BHOJ RAJ SHARMA

DEPARTMENT OF CARDIOLOGY
DAYANAND MEDICAL COLLEGE & HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	TO STUDY DIFFERENT CLINICAL PHENOTYPES AND SHORT TERM FOLLOW UP IN PATIENTS PRESENTING WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION
For the degree of	DM CARDIOLOGY
Name of the candidate	Dr. Bhoj Raj Sharma
Supervisor	Dr. Gurpreet S Wander, Professor & Head, Department of Cardiology, Dmch, Ludhiana.
Co-supervisors	Dr. Gautam Singal, Assistant Professor, Department of Cardiology, Dmch, Ludhiana.
Institution	Dayanand Medical College & Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: In recent years, Heart failure with preserved ejection fraction (HFpEF) has been suggested to be a heterogeneous disease .The identification of different phenotypes of HFpEF hereby becomes imperative in deciding the effective diagnostic strategies. Previous studies suggest paucity of data related to identification of different clinical phenotypes of HFpEF. This study will be the aimed to identify different clinical phenotypes of HFpEF and short term follow up.

Aim of Study: 1) To study different clinical phenotypes of patient with heart failure with preserved ejection fraction.

2) To establish the correlation of studied clinical phenotypes with patient outcome in heart failure with preserved ejection fraction.

Materials & Methods: All the patients with different clinical phenotypes fulfilling criteria for heart failure with preserved ejection fraction presenting to OPD and emergency department will be enrolled in this study and short term follow up will be assessed.

Clinical Significance: Prevalence of heart failure with preserved ejection fraction is on rising trend due to improvement in early diagnosis and new treatment approaches. So this disease entity needs more study in future and needs to assess clinical outcome with different clinical phenotypes.

Keywords: Heart failure with preserved ejection fraction, H_2FPEF score , HFA-PEFF diagnostic algorithm ,KCCQ Questionarre

(Signature) Candidate	(Signature) Co-Supervisor	(Signature) Supervisor	(Signature) Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"TO STUDY DIFFERENT CLINICAL PHENOTYPES AND SHORT TERM FOLLOW UP IN PATIENTS PRESENTING WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION"** exist in the Department of Cardiology, DMC&H, and Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate himself under our supervision and guidance.

Supervisor

Dr. Gurpreet Singh Wander
Professor & Head
Department of Cardiology
DMCH, Ludhiana

Co-Supervisors

Dr. Gautam Singal
Assistant Professor
Department of Cardiology
DMCH,Ludhiana

Head of the Department

Dr. Gurpreet Singh Wander
Professor & Head
Department of Cardiology
DMCH, Ludhiana

Place : LUDHIANA

Date : 28/12/2022

APPROVAL PROFORMA
BY RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr. Bhoj Raj Sharma
Department	Cardiology
Topic of Thesis	TO STUDY DIFFERENT CLINICAL PHENOTYPES AND SHORT TERM FOLLOW UP IN PATIENTS PRESENTING WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION
Likely date of appearing in PG examination	March, 2025
Date of enrollment	30 April 2022
Name of Head of Department	Dr. Gurpreet Singh Wander
1) Supervisor **2) Co-Supervisor**	Dr. Gurpreet Singh Wander Dr. Gautam Singal
Signature of Members of Research Committee with Stamp	**Signature of Members of Ethics Committee with Stamp**
Dr. Harpreet Kaur (Professor & Head, Pathology)	Mr. R K Sharma (Legal Expert)
Dr. Jaspal Singh (Professor & Head, Surgery)	Dr. Ramit Mahajan (Associate Professor, Gastroenterology)
Dr. Dinesh Gupta (Professor & Head, Medicine)	Dr. Anu Sharma (Professor, Anatomy)
Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)	Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)
Dr. Gurpreet S Wander (Vice Principal)	Dr. Gurpreet S Wander (Vice Principal & Professor & Head, Cardiology)
	Dr. Gagandeep Singh (Secretary, Ethics Committee Professor & Head, Neurology)

Approved: Yes / ~~No~~

Dr. Sandeep Puri
Chairperson
Research Committee

Chairperson
Research Committee

Approved: Yes / ~~No~~

Prof. Arvind Malhotra
Chairperson
Ethics Committee

Chairperson
Ethics Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	Dr. BHOJ RAJ SHARMA ADDRESS- # 344 SECTOR-24/B DALIP NAGAR, STREET NUMBER-06 MANDI GOBINDGARH PUNJAB (147301)
2	NAME OF THE INSTITUTE	DAYANAND MEDICAL COLLEGE AND HOSPITAL LUDHIANA
3	COURSE OF STUDY AND SUBJECT	DM CARDIOLOGY
4	DATE OF ADMISSION OF COURSE	30TH APRIL, 2022
5	TITLE OF THE TOPIC	TO STUDY DIFFERENT CLINICAL PHENOTYPES AND SHORT TERM FOLLOW UP IN PATIENTS PRESENTING WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Heart failure is a clinical syndrome consisting of cardinal symptoms of breathlessness, ankle swelling, and fatigue that may be accompanied by signs elevated jugular venous pressure, pulmonary crackles, and peripheral oedema. It is due to a structural and/or functional abnormality of the heart that results in elevated intracardiac pressures and/or inadequate cardiac output at rest and/or during exercise. Traditionally, HF has been divided into distinct phenotypes based on the measurement of left ventricular ejection fraction. Reduced LVEF is defined as ≤40%, i.e. those with a significant reduction in LV systolic function. This is designated as heart failure with reduced ejection fraction(HFrEF). Patients with a LVEF between 41% and 49% have mildly reduced LV systolic function, i.e.heart failure with mid range ejection fraction.(HFmEF). Those with symptoms and signs of HF, with evidence of structural and/or functional cardiac abnormalities and/or raised natriuretic peptides (NPs), and with an LVEF ≥50%, are heart failure with preserved ejection fraction(HFpEF). [1] . Despite the marked progresses in the treatment of cardiovascular disease over the past decades, the incidence and prevalence of HF have not decreased. Heart failure affects approximately 26 million people worldwide[2] and the projections are even more worrying as it is expected that by 2030 more than 8 million people will have this condition, accounting for a 46 % increase in its prevalence.[3]

Earlier from a pathophysiologic point of view, the primary abnormality “Heart failure with normal or preserved ejection fraction” (HFpEF) was traditionally thought to be diastolic dysfunction (DHF) which was associated with both impaired LV relaxation and decreased LV compliance.[4-9]

Different clinical profiles of HFpEF have been gradually identified. For example, HFPEF has been associated with pulmonary arterial hypertension, aging , hypertension, coronary artery disease and obesity . The most significant comorbidities leading to structural and functional remodeling of the heart includes atrial fibrillation , anaemia,

COPD , fraility, diabetes , obstructive sleep apnea and chronic kidney disease.

. Adding to the complexity of HFpEF is the fact that these patients often have more than one pathophysiology of HFpEF that may result in different clinical presentations, culminating in the emerging of different phenogroups in this clinical syndrome.[10]

HFpEF is becoming more common in developed countries, accounting for more than half of all heart failure cases. Despite the fact that patients with HFpEF have a lower risk of death than those with HFrEF, absolute mortality is high and rising, signaling the start of a global pandemic. HFrEF has seen significant improvements in terms of mortality and functional capacity, while heart failure with retained ejection fraction still remains a therapeutic challenge (HFpEF). The phenotypic variability identified in this disorder is one of the significant problems and barriers to successfully treat HFpEF. [11-12]

In recent years, Heart failure with preserved ejection fraction (HFpEF) has been suggested to be a heterogeneous disease with high mortality and morbidity. The identification of different phenotypes of HFpEF hereby becomes imperative in deciding the effective diagnostic strategies.

Previous studies suggest paucity of data related to identification of different clinical phenotypes of HFpEF.

Therefore, in the present study we will study different clinical phenotypes of patient presenting with Heart failure with preserved ejection fraction and short term clinical outcome.

6.2 REVIEW OF LITERATURE

- Shah SJ et al in his study from North America in 2015 were the first to identify phenogroups of a heart disease, and the first to use the machine learning technique as an approach to solve the heterogeneity of a cardiovascular syndrome by phenotype analysis[13,15] They prospectively studied 397 patients with HFpEF and performed detailed clinical, laboratory, ECG, and echocardiographic phenotyping of the study participants. They proposed a classification based on the biological phenotypes which seemed to be better in describing the underlying pathomechanisms of HFpEF. The three identified biological phenogroups according to their classification includes:
  1. Natriuretic peptide deficiency syndrome: younger subjects with moderate diastolic dysfunction and relatively normal BNP.
  2. Extreme cardiometabolic syndrome: obese, diabetic subjects with a high prevalence of obstructive sleep apnea.
  3. Right ventricle-cardio-abdomino-renal syndrome: older subjects with significant chronic kidney disease and cardiopulmonary comorbidities

     They also mentioned that both 2 and 3 phenogroups were associated with poor patient outcomes. The HFpEF phenogroup classification, including its ability to stratify risk, was successfully replicated in a prospective validation cohort (n=107). hence they cocluded that Phenomapping results in a novel classification of HFpEF. Statistical learning algorithms applied to dense phenotypic data may allow improved classification of heterogeneous clinical syndromes, with the ultimate goal of defining therapeutically homogeneous patient subclasses.
- There are four clinically distinct phenotypes of HFpEF that have been described by Samson R et al in 2016.[14] Their categorization recognizes the diversity of the population and the necessity for a personalized approach. These include:
  1. Aging phenotype

2. Obesity phenotype
3. Pulmonary hypertension (PH) phenotype
4. Coronary artery disease (CAD) phenotype.

   The various comorbities associated with different phenotypes includes atrial fibrillation, aneamia , COPD ,diabetes ,obstructive sleep apnea, chronic kidney disease.

- Hedman ÅK et al in 2020 aimed to derive HFpEF phenotype-based groups (’phenogroups’) based on clinical and echocardiogram data using machine learning, and to compare clinical characteristics, proteomics and outcomes across the phenogroups.[16] They applied model-based clustering to 32 echocardiogram and 11 clinical and laboratory variables collected in stable condition from 320 HFpEF outpatients in the Karolinska-Rennes cohort study. **They** identified following six phenogroups:
  1) Younger, risk factors such as hypertension, CAD and diabetes, larger left ventricular volumes, and CKD.
  2) Older, less hypertrophy but worse left ventricular and right ventricular systolic function and more severe HF, and notably high prevalence of COPD.
  3) Younger, male, obesity, less left and right diastolic and systolic function, and milder HF.
  4) Male, hypertension, left ventricular hypertrophy, left atrial enlargement and AF.
  5) Older, female, hypertension, CAD, large left side but good right ventricular function.
  6) Older, female, low BMI, hypertension, AF and right-sided failure.

  Significant differences in the prevalence of concomitant atrial fibrillation (AF), anaemia and kidney disease were observed. The composite end point was significantly different between phenogroups, at short-term (100 days), mid-term (18 months) and longer-term follow-up (1000 days). Phenogroup 2 was older,

with poorer diastolic and right ventricular function and higher burden of risk factors as AF (85%), hypertension (83%) and chronic obstructive pulmonary disease (30%). In this group a third experienced the primary outcome to 100 days, and two-thirds to 18 months (HR (95% CI) versus phenogroups 1, 3, 4, 5, 6.

- Recently in 2021, Nguyen NT et al[17] conducted an observational study on 477 patients diagnosed with HFpEF from seven hospitals in Southern Vietnam. They reported that valvular heart disease (VHD) was the leading cause of heart failure (35.9%). 78.6% had at least two comorbidities, mostly hypertension (68.6%). Older patients (≥65 years) were more likely to be females and had multimorbid conditions including hypertension, diabetes, coronary artery disease (CAD), dyslipidemia and chronic kidney disease and were more frequently prescribed statin. Younger individuals (<65 years) were associated with higher mineralocorticoid antagonist uptake and VHD . Prescription rate for renin-angiotensin-aldosterone system inhibitor, beta blocker, mineralocorticoid antagonist, and loop diuretic was 72.5%, 59.1%, 43.0%, and 60.6%, respectively. They identified four phenotypes, including the
- Lean/ elderly/multimorbid
- Congestive/metabolic
- CAD-induced
- Younger/atrial fibrillation (AF)/VHD).

  The novel phenotype “younger/AF/VHD” exhibited high symptom burden and poor functional capacity despite being the youngest and least multimorbid. The “lean/elderly/multimorbid” phenotype demonstrated the highest symptom severity and inhospital mortality. Hence they concluded that the younger, predominantly female population were associated with high disease burden. The four novelly identified phenotypes provide contemporary and pragmatic insights into a phenotype-guided approach, exclusively targeting the study population.

6.3 AIM AND OBJECTIVE OF THE STUDY

1) To study different clinical phenotypes of patient with heart failure with preserved ejection fraction.
2) To establish the correlation of studied clinical phenotypes with patient outcome in heart failure with preserved ejection fraction.

7. MATERIALS AND METHODS

7.1 SOURCE OF DATA

The present study will be a single centre, prospective observational study.

The study will be conducted in Department of Cardiology, Hero DMC Heart Institute.

SAMPLE SIZE

Sample size would be total number of heart failure patients with preserved ejection fraction presenting to the Department of Cardiology, Hero DMC Heart Institute during the defined duration of study.

7.2 METHOD OF COLLECTION OF DATA

- **PATIENT SELECTION:** All the patients diagnosed with heart failure with preserved ejection fraction during the study duration will be collected fulfilling the inclusion and the exclusion criteria.
- **DATA COLLECTION:** Demographic features like age, presenting symptoms, medical and behavioral history and functional status will be obtained through direct interview and physical examination. Investigations, risk factors and comorbidities will be taken from medical records or newly identified, included coronary artery disease (CAD), hypertension (HTN), atrial fibrillation/atrial flutter (AF), diabetes mellitus (DM), chronic kidney failure (CKD), obesity, chronic obstructive pulmonary disease, obstructive sleep apnea, anaemia and pulmonary hypertension.

All the heart failure patients diagnosed with preserved ejection fraction HFpEF according to our diagnostic criteria will be enrolled in the study.

Clinical variable	Values	Points
Heavy	BMI >30kg/m2	2
Hypertensive	2 or more antihypertensives	1
Atrial fibrillation	Paroxysmal or persistant	3
Pulmonary hypertension	Pulmonary artery systolic pressure >35mmHg	1
Elderly	>60 years	1
Filling pressures	Doppler echocardiographic E/e' 9	1

H_2FPEF SCORE

MAJOR	septal e <7cm/s or lateral e <10cm/s or average E/e >15 or TR velocity >2.8m/s(PASP >35mmHg)	LAVI >34ml/m2 Or LVMI >149/122g/m2 and RWT >0.42	NT proBNP >220pg/ml or BNP >80pg/ml	NT proBNP >660pg/ml or BNP >240pg/ml
MINOR	Average E/e 9-14 or GLS <16%	LAVI 29-34ml/m2 or LVMI >115/95g/m2 Or RWT >0.42 Or LV wall thickness >12mm	NT proBNP 125-220 pg/ml or BNP 35-80pg/ml	NT proBNP 365-660pg/ml or BNP 105-240pg/ml

HFA-PEFF score

Major criteria : 2 points

Minor criteria : 1 point

SCORE >5 =HFpEF

INCLUSION CRITERIA:

Heart failure patients with preserved ejection fraction HFpEF will be defined as satisfying all three criteria:

(1) Age ≥ 18years

(2) EF ≥50%

(3) One of the following criteria:

(a) Previously documented NT-proBNP ≥ 125 pg/ml

(b) Diagnosed with heart failure using Framingham criteria, and a previously documented NTproBNP

≥125 pg/ml

Framingham Diagnostic Criteria for Heart Failure

Major Criteria	Minor Criteria
Acute Pulmonary Edema	Ankle Edema
Cardiomegaly	Dyspnea on exertion
Hepatojuglar Reflex	Hepatomegaly
Neck Vein Distension	Nocturnal Cough
Paroxysmal Nocturnal Dyspnea/ Orthopnea	Pleural Effusion
Rales	Heart Rate > 120
Third Heart Sound	

Heart failure is diagnosed when two major criteria or one major and two minor criteria are met.

(4) Diagnosed as HFpEF by a trained cardiologist at each enrolment site

EXCLUSION CRITERIA:

The exclusion criteria included all those patients presenting with:

1. End-stage renal (creatinine clearance < 30ml/min by cock croft - --gault formula)
2. Severe hepatic impairment (Child Pugh class B or C)
3. Prior documented EF <50%
4. Life expectancy <1 year due to noncardiac etiologies.
5. Pregnancy or lactation
6. Patients with uncontrolled blood pressure
7. Concurrent enrolment in any other trial

DURATION OF STUDY/NO. OF CASES

All patients fulfilling criteria of heart failure with preserved ejection fraction coming to OPD and emergency department of Hero DMC heart Institute during 1 year and their follow up for 6 months.

OUTCOME: Different clinical phenotypes of patient presenting with heart failure with preserved ejection fraction and their short term outcome will be studied

STATISTICAL ANALYSIS:

Data will be described in terms of range; mean ±standard deviation (± SD), frequencies (number of cases) and relative frequencies (percentages) as appropriate. For comparing categorical data, Chi square ($\chi 2$) test will be performed and fisher exact test will be used when the expected frequency is less than 5. A probability value (*p* value)less than 0.05 will be considered statistically significant. All statistical calculations will be done using (Statistical Package for the Social Science) SPSS 21version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

No.

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Yes, Attached herewith.

8. LIST OF REFERENCES

1. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021;42:3599-3726.
2. Ponikowski P, Anker SD, AlHabib KF, Cowie MR, Force TL, Hu S, et al. Heart failure: preventing disease and death worldwide. ESC heart failure. 2014;1:4-25.
3. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Heart disease and stroke statistics—2016 update: a report from the American Heart Association. circulation. 2016;133:e38-60.
4. Owan TE, Hodge DO, Herges RM, Jacobsen SJ, Roger VL, Redfield MM. Trends in prevalance and outcome of heart failure with preserved ejection fraction. N Engl J Med 2006;355:251–9
5. Hogg, K, Swedberg, K, McMurray, J. Heart failure with preserved left ventricular systolic function; epidemiology, clinical characteristics, and prognosis. J Am Coll Cardiol 2004; 43:317
6. Zile MR, Brutsaert DL. New concepts in diastolic dysfunction and diastolic heart failure: Part I: diagnosis, prognosis, and measurements of diastolic function. Circulation. 2002;105:1387-93.
7. Shah AM, Solomon SD. Phenotypic and pathophysiological heterogeneity in heart failure with preserved ejection fraction. Eur Heart J. 2012;33:1716–7
8. Borlaug BA, Paulus WJ. Heart failure with preserved ejection fraction: pathophysiology, diagnosis, and treatment. Eur Heart J. 2011;32:670–9.
9. Bench T, Burkhoff D, O'Connell JB, Costanzo MR, Abraham WT, St John Sutton M, et al. Heart failure with normal ejection fraction: consideration of mechanisms other than diastolic dysfunction. Current heart failure reports. 2009;6:57-64.

10. Shah SJ, Katz DH, Deo RC. Phenotypic spectrum of heart failure with preserved ejection fraction. Heart Fail Clin. 2014;10:407-18.
11. Mesquita ET, Jorge AJ, Souza Junior CV, Cassino JP. Systems biology applied to heart failure with normal ejection fraction. Arq Bras Cardiol. 2014;102:510-7.
12. Joyner MJ. Precision medicine, cardiovascular disease and hunting elephants. Prog Cardiovasc Dis. 2016;58:651-60.
13. Shah SJ, Katz DH, Selvaraj S, Burke MA, Yancy CW, Gheorghiade M, et al. Phenomapping for novel classification of heart failure with preserved ejection fraction. Circulation. 2015;131:269-79.
14. Samson R, Jaiswal A, Ennezat PV, Cassidy M, Le Jemtel TH. Clinical phenotypes in heart failure with preserved ejection fraction. J Am Heart Assoc. 2016;5.
15. Shah SJ. 20th Annual Feigenbaum Lecture: echocardiography for precision medicine-digital biopsy to deconstruct biology. J Am Soc Echocardiogr. 2019;32:1379–1395.e2.
16. Hedman ÅK, Hage C, Sharma A, Brosnan MJ, Buckbinder L, Gan LM, et al. Identification of novel pheno-groups in heart failure with preserved ejection fraction using machine learning. Heart. 2020;106:342-9.
17. Nguyen NT, Tran DT, Le An P, Van Hoang S, Nguyen HA, Chau HN. Clinical phenotypes and age-related differences in presentation, treatment, and outcome of heart failure with preserved ejection fraction: a Vietnamese multicenter research. Cardiology Research and Practice.2021.

PROFORMA

Date:_____

1. DEMOGRAPHIC CHARACTERISTICS

Name.		**Age (years)**	
Date of Birth		**Sex**	**M / F / Other**
Date of visit		**Phone no.**	
Address			
Occupation			
Height (cm)		**Weight (kg)**	

SIGNATURE OF CANDIDATE SIGNATURE OF SUPERVISOR

2. HISTORY

1. Personal History:

1. Alcohol Intake: Yes/No
   If yes, mention quantity: ……
2. Smoking: Yes/No
   If yes, mention quantity…….
3. Allergies: Yes/No
   If yes, mention name of drug……
4. Pacemaker/Other devices: Yes/No
   If yes, mention name of the device…….
5. Others:

2. Medical history:

1. **Diabetes:** Yes/ No

   If yes,

   Treatment:

2. **Hypertension:** Yes/ No

   If yes,

   Treatment:

3. **Coronary heart disease:** Yes/ No

   If yes,

Treatment:

4. **Neurological disease:** Yes/ No

   If yes,

   Treatment:

5. **Respiratory disease:** Yes/ No

   If yes,

   Treatment

SIGNATURE OF CANDIDATE SIGNATURE OF SUPERVISOR

3. GENERAL EXAMINATION

Parameter		Remarks		Parameter		Remarks
Built		Well-built/Lean/Obese		Nourishment		Adequate/Under/Over
Pallor	Clubbing	Cyanosis	Edema	Icterus	Lymphadenopathy	
Y / N	Y / N	Y / N	Y / N	Y / N	Y / N	

Vital Signs

Parameter	Reading	Parameter	Reading
Blood Pressure (mmHg)		Temperature (˚C)	
Pulse rate (bpm)		Respiratory rate (per min)	

SYSTEMIC EXAMINATION

Organ/System	Nor	AbN	NE
Cardiovascular			
Abdomen			
Respiratory			
Skin			
Extremities			

Nor=Normal; AbN=Abnormal; NE=Not Examined

SIGNATURE OF CANDIDATE SIGNATURE OF SUPERVISOR

4. LABORATORY INVESTIGATIONS

HAEMATOLOGY		BIOCHEMISTRY	
Test	Value	Test	Value
Hemoglobin (g/dl)		SGPT (IU/L)	
TLC (cells/cc)		SGOT (IU/L)	
Neutrophils (%)		Se. Bilirubin (mg/dl)	
Lymphocytes (%)		Total Se. Protein (g/dl)	
Basophils (%)		Se. Albumin (g/dl)	
Eosinophils (%)		Se. Globulin (g/dl)	
Platelets (cells/cc)		Se. Creatinine (mg/dl)	
ESR		Blood urea (mg/dl)	
		Uric Acid	

SIGNATURE OF CANDIDATE SIGNATURE OF SUPERVISOR

BIOCHEMISTRY (contd.)]	
Test	**Value**
Serum Na+ (mEq/L)	
Serum K+ (mEq/L)	
Fasting/Random Blood Sugar (mg/dl)	
Total Cholesterol (mg/dl)	
Triglyceride (mg/dl)	
LDL-C (mg/dl)	
HDL-C (mg/dl)	
VLDL-C (mg/dl)	
Serum iron	
Serum transferrin saturation	
Total iron binding capacity	
Serum ferritin	
T3	
T4	
TSH	

SIGNATURE OF CANDIDATE SIGNATURE OF SUPERVISOR

LABORATORY INVESTIGATIONS (contd.)

ECG

RATE

Atrial fibrillation yes/no

Type of atrial fibrillation

Paroxysmal

Persistant

Permanent

Echocardiography parameters

a. Left Ventricular Ejection Fraction (LVEF in %)
b. Mitral E wave velocity (E in cm/s)
c. Mitral A wave velocity (A in cm/s)
d. Mitral E/A wave velocity (E/A)
e. Mitral annular velocity (E' in cm/s)
f. Mitral wave velocity / Mitral annular velocity (E/E')
g. Peak atrial longitudinal strain

5. **NT-proBNP:**

6. **Chest X-ray findings:**

SIGNATURE OF CANDIDATE SIGNATURE OF SUPERVISOR

7. Concomitant treatment:

8. 6-minute walk test finding:

9. KCCQ evaluation

10. Number of episodes of hospitalisation during follow up period

Number of days during each hospitalisation

Patient outcome

11. List of medications

SIGNATURE OF CANDIDATE SIGNATURE OF SUPERVISOR

INFORMED PATIENT CONSENT

Date: _____

I……..D/o, W/o, S/o……. ……am willing to participate in the study **"TO STUDY DIFFERENT CLINICAL PHENOTYPES AND SHORT TERM FOLLOW UP IN PATIENTS PRESENTING WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

……. ……

Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य **"TO STUDY DIFFERENT CLINICAL PHENOTYPES AND SHORT TERM FOLLOW UP IN PATIENTS PRESENTING WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____

गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

“TO STUDY DIFFERENT CLINICAL PHENOTYPES AND SHORT TERM FOLLOW UP IN PATIENTS PRESENTING WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION” ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।
ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ